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Nighttime mean arterial pressure is associated with left ventricular hypertrophy in white-coat hypertension

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Abstract

White-coat hypertension (WCH) is associated with increased cardiovascular risks. To investigate the relationship between WCH and left ventricular hypertrophy (LVH), the authors recruited 706 participants who underwent anthropometric measurements, blood laboratory analysis, 24h ambulatory blood pressure monitoring (ABPM), and echocardiography. The authors defined WCH as elevated office BP but normal ABPM over 24h, daytime, and nighttime periods. The authors compared the proportion of LVH between the true normotension (NT) and the WCH population, and further assessed the associations between BP indexes and LVH in the two groups, respectively. The proportion of LVH was significantly higher in the WCH group than in NT participants (19.70% vs. 13.12%, $P = .036$). In the NT group, 24h SBP, 24h PP, daytime SBP, daytime PP and SD of nighttime SBP were associated with LVH after adjustment for demographic and blood biochemical data (all $P < .05$). In the WCH population, LVH was associated with 24h SBP, nighttime SBP, nighttime MAP, and office SBP after adjustment (all $P < .05$). However, on forward logistic regression analysis with all the BP indexes listed above, only 24h SBP (OR = 1.057, 1.017–1.098, $P < .001$) in the NT group, and nighttime MAP (OR = 1.114, 1.005–1.235, $P < .05$) and office SBP (OR = 1.067, 1.019–1.117, $P < .001$) in the WCH group were still significantly associated with LVH. Our study suggests that the proportion of LVH is higher in WCH patients than in the NT population. Furthermore, elevated nighttime MAP and office SBP may play critical roles in the development of LVH in the WCH population.

KEYWORDS
ambulatory blood pressure monitoring, echocardiography, left ventricular hypertrophy, nighttime blood pressure, white-coat hypertension

Xiangyu Yang and Yuan Yuan contributed equally to this review paper.

1 | INTRODUCTION

White-coat hypertension (WCH) is a specific condition in which patients have normal blood pressure (BP) during ambulatory blood pressure monitoring (ABPM) or home blood pressure monitoring (HBPM), but elevated BP in medical settings (office blood pressure or OBP). According to the results of PAMELA study, the prevalence of WCH was up to 15% in the general population, and even higher in hypertensive patients.[1] WCH was initially regarded as a harmless condition. However, over the past two decades it has been proved to be associated with dysmetabolic risk factors profiles, subclinical organ damages, a greater incidence of new onset of cardiovascular diseases, and poorer cardiovascular outcomes, compared with the normotension (NT) population.[2]

There are discrepancies in the different guidelines regarding the most appropriate ABPM cut-off value to diagnose WCH. In the 2007 ESH/ESC guidelines, a mean awake ABPM value < 135/85 mm Hg was proposed to distinguish WCH from sustained hypertension.[3] However, nighttime BP has a closer association with target organ damage and cardiovascular prognosis. Therefore, some guidelines suggested a 24h ABPM of 130/80 mm Hg as the cut-off value.[4,5] Nevertheless, in the 2017 ACC/AHA guidelines, a daytime ABPM value < 130/80 mm Hg was still recommended for diagnosing WCH.[6] As the definitions recommended by different guidelines vary, the inclusion criteria applied in published WCH studies also differ from each other. Earlier guidelines did not emphasize the nighttime ambulatory blood pressure in the definition of WCH, which led to the majority of earlier studies enrolling populations with abnormal nighttime BP. In addition, there is minimal published research focusing on WCH patients, diagnosed by elevated OBP but normal ambulatory BP in all time periods (24h, daytime and nighttime). Therefore, in this study, we recruited participants with normal ambulatory BP in all time periods, aiming to assess the relationship between WCH and left ventricular hypertrophy (LVH), and to explore the associations between BP indexes and LVH in WCH and NT participants.

2 | POPULATION AND METHODS

2.1 | Study population

This cross-sectional study included participants with normal 24h ABPM from both the inpatient and outpatient departments of West China Hospital, Sichuan University. All participants were recruited from January 2020 to December 2021. Participants with normal 24h SBP/DBP (< 130/80 mm Hg), normal daytime SBP/DBP (< 135/85 mm Hg), and normal nighttime SBP/DBP (< 120/70 mm Hg) were enrolled in our study. Patients with one or more of the following were excluded: (1). history of cardiovascular events; (2). history of hypertension or diabetes mellitus; (3). diagnosed cardiomyopathy or valvular heart disease; (4). history of atrial fibrillation; (5). history of malignant tumor; (6). patients using drugs affecting BP measurement; and (7). incomplete data. The final study population included 706 participants. The participant selection process was shown in Figure 1. The study procedures were approved by the Medical Ethics Committee of the West China Hospital of Sichuan University. All participants provided written informed consent before recruitment.

2.2 | Data collection

Demographic data were acquired using a questionnaire regarding age, sex, height, weight, smoking and alcohol drinking status. Laboratory analyses including fasting blood glucose (FBG), creatinine (CREA), uric acid (URIC), triglycerides (TG), total cholesterol (TC), high-density lipoprotein-cholesterol (HDL-C) and low-density lipoprotein-cholesterol (LDL-C) were performed in West China Hospital, Sichuan university.

2.3 | OBP and 24h ABPM

OBP measurement for each participant was obtained by Omron HBP-1100 in a sitting position in a clinical environment, before performing ABPM. Three effective readings were averaged before the analysis. 24h ABPM was performed using the validated SpaceLabs 90217 devices (SpaceLabs Medical, Redmond, WA, USA). An appropriate size cuff was placed on each participant's nondominant arm. The BP was measured every 20 min during the daytime (06:00-–22:00 h) and every 60 min during the nighttime (22:00–-06:00 h). Participants were asked to record the exact timepoint when they woke up, went to bed, or participated in any noticeable activities. Office SBP ≥140 mm Hg or office DBP ≥90 mm Hg was defined as elevated. WCH was defined as elevated OBP but normal ABPM values in all 24h, daytime, and nighttime periods.[7]

2.4 | Echocardiography

Echocardiography was performed by experienced operators from West China Hospital, Sichuan University, using the GE VividE9 color Doppler ultrasound detector with an M5S probe (GE Healthcare, Horten, Norway). Left ventricular end-diastolic diameter (LVEDD), end-diastolic interventricular septal wall thickness (IVST), and end-diastolic left ventricular posterior wall thickness (LVPWT) were assessed by the linear method with M-mode tracing. Left ventricular mass (LVM) was calculated as .8×1.04×[(IVST+LVPWT+LVEDD)3-LVEDD3]+.6. Body surface area (BSA) was calculated as .0061×height (cm)+.0125×weight (kg)-.1529. Left ventricular mass index (LVMI) was then calculated as LVM/BSA. Left ventricular hypertrophy (LVH) was define as LVMI > 115 in males or LVMI > 95 in females, respectively.[8]

2.5 | Statistical analysis

Kolmogorov–Smirnov test was used to test the normality of the distribution. Categorical data are presented as frequencies and

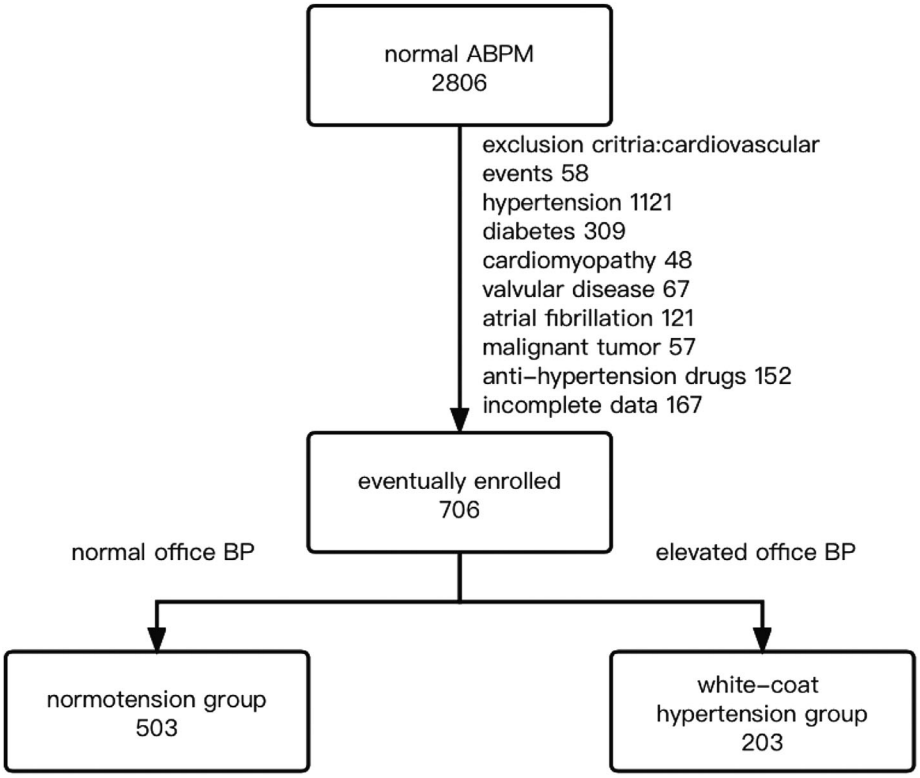

FIGURE 1 Flow chart

percentages. Continuous variables are presented as mean ± SD if normally distributed and median (IQR) if skewed. The study population was divided into subgroups according to OBP (NT vs. WCH) and LVMI (non-LVH vs. LVH). Differences regarding demographic and clinical characteristics between the two groups were tested by independent t-test for normally distributed data, nonparametric Mann–Whitney or Wilcoxon test for skewed data, and Chi-square test for categorical data. The associations between each BP index and LVH were analyzed by univariate and multivariate logistic regression analysis and the results were reported as odds ratio (OR) with 95% confidence intervals (95% CIs). Univariate and multivariate linear regression analysis was performed to test the association between each BP index and LVMI. The regression coefficient β with 95% CIs were calculated to represent to what extent were BP indexes related to LVMI. Statistical analysis was performed using SPSS version 23.0 (IBM Corp., Armonk, New York, USA), and P value < .05 was considered as statistically significant.

3 | RESULTS

3.1 | Baseline characteristics of the participants

A total of 706 participants with normal ABPM were enrolled in our study; the median age was 53.39 years and 38.24% were males. The normotension (NT) group included 503 (71.25%) participants with both normal ABPM and OBP. The white-coat hypertension (WCH) group included 203 (28.75%) participants with normal ABPM but elevated OBP. The percentage of female, age, BMI, FBG, TC, HDL-C and LVMI were higher in the WCH group than in the NT group (all $P < .05$). In contrast, no significant differences were found in CREA, URIC, TG or LDL-C levels between the two groups (all $P > .05$, Table 1). The proportion of LVH was significantly higher in the WCH group than in the NT group (19.70% and 13.12%, respectively, $P = .036$, Table 1).

3.2 | BP measurements in participants with and without LVH

3.2.1 | NT group

In the NT group, participants with elevated LVMI were more likely to be nondipper and have higher office SBP, office PP, 24h SBP, 24h PP, daytime SBP, daytime PP, SD of daytime SBP, nighttime SBP, nighttime PP, and SD of nighttime SBP than those with normal LVMI (all $P < .05$). However, nighttime DBP dip, and nighttime MAP dip were lower in participants with LVH (all $P < .05$, Table 2).

3.2.2 | WCH group

Compared with non-LVH participants, those with LVH were more likely to have higher office SBP, office PP, 24h SBP, 24h PP, daytime PP, nighttime SBP, nighttime MAP, and nighttime PP (all $P < .05$). Nevertheless, office HR was significantly lower in LVH participants (all $P < .05$). No differences were found in the other indexes presented (all $P \geq .05$, Table 2).

TABLE 1 Baseline characteristics of NT and WCH

Characteristics	Overall ($n = 706$)	NT ($n = 503$)	WCH ($n = 203$)	*P* value
Male, *n* (%)	270 (38.24)	204 (40.56)	66 (32.51)	.049*
Age (year)	53.39±16.14	52.19±16.41	56.36±15.09	.002#
BMI (kg/m^2)	23.26±3.40	23.08±3.48	23.71±3.15	.027*
Smoking, *n* (%)	109 (15.44)	79 (15.71)	30 (14.78)	.818
Alcohol, *n* (%)	94 (13.31)	68 (13.52)	26 (12.81)	.903
FBG (mmol/L)	5.21±.86	5.16±.85	5.35±.89	.016*
CREA (mmol/L)	72.00±14.93	72.33±15.14	71.15±14.39	.404
URIC (mmol/L)	311.70±83.82	313.85±86.98	306.15±75.05	.298
TG (mmol/L)	1.44±.96	1.43±.99	1.44±.89	.906
TC (mmol/L)	4.62±.99	4.54±1.01	4.83±.93	.002#
HDL-C (mmol/L)	1.39±.40	1.36±.38	1.47±.45	.005#
LDL-C (mmol/L)	2.71±.85	2.66±.85	2.82±.84	.054
LVMI (g/m^2)	85.96±17.33	84.14±18.54	89.68±19.19	.008#
LVH, *n* (%)	106 (15.01)	66 (13.12)	40 (19.70)	.036*

* represents $P < .05$, # represents $P < .01$.
Values are expressed as mean±SD or number of participants (%).
Abbreviations: BMI, body mass index; FBG, fasting blood glucose; CREA. Creatinine; URIC, uric acid; TG, triglycerides; TC, total cholesterol; HDL-C, high-density lipoprotein-cholesterol; LDL-C, low-density lipoprotein-cholesterol; LVMI, left ventricular mass index; LVH, left ventricular hypertrophy.

3.3 | BP indexes associated with LVH in the NT and WCH group

3.3.1 | NT group

Both univariate and multivariate logistic regression analyses were performed in our study. BP indexes that were significantly different between LVH and non-LVH group by t-test in either the NT group or WCH group were selected as independent variables. In univariate logistic regression analysis, 24h SBP, 24h PP, daytime SBP, daytime PP, SD of daytime SBP, nighttime SBP, nighttime PP, SD of nighttime SBP, office SBP, office PP, nighttime DBP dip, and nighttime MAP dip were associated with LVH in the NT group (model 1, all $P < .05$). The 24h SBP, 24h PP, daytime SBP, daytime PP, and SD of nighttime SBP were still significantly associated with LVH after adjustment for age, sex, smoking status, drinking status, BMI, FBG, CREA, URIC, TG, TC, HDL-C, and LDL-C (model 2, all $P < .05$). In contrast, the other BP indexes were not. Daytime PP was excluded after collinearity diagnostics, then the four BP indexes listed above were substituted into the multivariate forward logistic regression model along with all the covariates used in Model 2. Only 24h SBP could enter the model (model 3, OR = 1.057, 1.017 to 1.098, $P < .001$), whereas 24h PP, daytime SBP and daytime PP could not (Table 3).

3.3.2 | WCH group

In the WCH group, 24h SBP, 24h PP, daytime PP, nighttime SBP, nighttime MAP, nighttime PP, office SBP, office PP, and office HR were related to LVH in univariate logistic regression (model 1, all $P < .05$). The 24h SBP, nighttime SBP, nighttime MAP, and office SBP were still associated with LVH when adjusted for age, sex, smoking status, drinking status, BMI, FBG, CREA, URIC, TG, TC, HDL-C, and LDL-C (model 2, all $P < .05$), whereas 24h PP, daytime PP, nighttime PP, office PP and office HR were not. After collinearity diagnostics, the four indexes listed above were substituted into the model together with all the covariates used in Model 2. Nighttime MAP and office SBP could enter the model (model 3, OR = 1.114, 1.005 to 1.235, $P < .05$ and OR = 1.067, 1.019 to 1.117, $P < .001$, respectively), whereas 24h SBP, and nighttime SBP could not (Table 4).

4 | DISCUSSION

For this study, we defined WCH as elevated OBP but normal ambulatory BP during all time periods. We observed a significantly higher proportion of LVH in the WCH population than in the NT population. Furthermore, 24h SBP was associated with LVH in normotensive participants, and nighttime MAP and office SBP were associated with the occurrence of LVH in the WCH group.

4.1 | White-coat hypertension and left ventricular hypertrophy

The term "white-coat hypertension" was first introduced by Pickering and coworkers[9] in 1988. During the past few decades, studies have yielded conflicting results on whether WCH has any clinical implications. Early studies found that WCH was not associated with increased cardiovascular risks. Taking LVH as an example, Chiara and

TABLE 2 Blood pressure characteristics of the participants by LVH

	NT			WCH		
Characteristics	**Non-LVH (*n* = 437)**	**LVH (*n* = 66)**	***P* value**	**Non-LVH (*n* = 163)**	**LVH (*n* = 40)**	***P* value**
Office SBP (mm Hg)	117.25±13.12	121.00±12.27	.030*	143.34±10.49	149.35±9.81	.001#
Office DBP (mm Hg)	75.27±8.12	73.79±8.03	.167	84.69±8.85	83.15±8.97	.327
Office MAP (mm Hg)	89.66±8.67	90.27±8.06	.592	104.99±8.14	105.98±7.37	.488
Office PP (mm Hg)	42.03±10.92	47.52±11.53	<.001#	58.67±13.54	66.20±13.55	.002#
Office HR (bpm)	77.94±12.12	76.14±15.33	.363	81.82±14.45	76.20±13.34	.027*
24h SBP (mm Hg)	106.65±8.38	110.12±8.63	.002#	115.69±6.52	118.35±5.82	.019*
24h DBP (mm Hg)	67.81±5.67	67.32±5.23	.503	70.18±5.51	68.93±5.43	.196
24h MAP (mm Hg)	81.55±5.35	82.73±5.26	.095	86.33±4.27	87.03±3.93	.347
24h PP (mm Hg)	39.02±7.07	43.00±7.83	<.001#	45.68±7.68	49.60±7.59	.004#
24h HR (bpm)	70.85±8.55	68.77±9.94	.073	69.53±8.56	68.38±7.61	.434
SD of 24h SBP	11.11±3.15	11.88±2.86	.062	13.83±2.79	14.08±2.58	.614
SD of 24h DBP	8.73±2.57	8.15±1.57	.075	9.41±1.91	8.90±1.58	.115
CV of 24h SBP (%)	10.38±2.71	10.78±2.39	.264	11.98±2.43	11.91±2.16	.297
CV of 24h DBP (%)	12.90±3.78	12.13±2.26	.109	13.40±2.49	12.95±2.32	.064
Daytime SBP (mm Hg)	110.16±10.45	113.42±9.53	.017*	121.17±7.13	123.23±6.18	.096
Daytime DBP (mm Hg)	70.74±6.23	69.70±5.95	.204	73.85±6.53	72.00±5.87	.104
Daytime MAP (mm Hg)	84.61±6.11	85.30±6.02	.388	90.28±4.86	90.60±4.05	.703
Daytime PP (mm Hg)	39.70±7.58	43.79±8.27	<.001#	47.42±8.35	51.25±8.19	.010*
Daytime HR (bpm)	74.58±9.13	72.29±10.34	.062	73.65±9.74	71.55±8.18	.209
SD of daytime SBP	9.78±2.85	10.90±2.87	.003#	12.09±2.63	12.97±2.48	.057
SD of daytime DBP	7.49±1.91	7.25±1.51	.249	8.07±1.97	7.80±1.61	.420
CV of daytime SBP (%)	9.03±4.90	9.59±2.28	.359	9.99±2.15	10.53±1.95	.150
CV of daytime DBP (%)	10.62±2.71	10.46±2.30	.651	10.97±2.66	10.91±2.42	.898
Nighttime SBP (mm Hg)	98.58±10.31	102.08±15.00	.017*	104.69±7.48	108.28±7.55	.007#
Nighttime DBP (mm Hg)	61.44±6.11	61.60±8.56	.859	62.96±4.73	62.68±5.63	.746
Nighttime MAP (mm Hg)	75.16±6.44	76.74±10.62	.093	78.28±4.52	79.93±4.94	.044*
Nighttime PP (mm Hg)	37.79±7.30	40.71±9.09	.004#	42.03±7.29	45.98±7.33	.002#
Nighttime HR (bpm)	63.03±9.35	60.61±12.65	.063	61.14±7.42	61.68±7.35	.683
SD of nighttime SBP	8.79±3.11	9.71±2.99	.026*	10.06±3.42	9.98±2.84	.894
SD of nighttime DBP	7.18±2.28	7.06±2.28	.697	7.57±2.54	7.60±2.38	.950
CV of nighttime SBP (%)	8.99±4.05	9.26±3.08	.605	9.62±3.18	9.24±2.58	.485
CV of nighttime DBP (%)	11.72±3.75	11.35±3.65	.447	12.03±3.90	12.11±3.50	.904
Nighttime SBP dip (%)	10.16±6.35	8.61±6.71	.067	13.54±5.16	12.14±5.18	.127
Nighttime DBP dip (%)	12.71±6.86	10.27±6.36	.007#	14.61±5.70	12.90±5.09	.085
Nighttime MAP dip (%)	10.84±6.11	8.68±6.22	.008#	13.23±4.63	11.80±4.41	.080
Non-dipper, n (%)	195 (44.62)	39 (59.09)	.034*	77 (47.24)	25 (62.50)	.112

*represents $P < .05$, # represents $P < .01$.

Values are expressed as mean±SD or number of participants (%).

Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; PP, pulse pressure; HR, heart rate; SD, standard deviation; CV, coefficient of variation.

TABLE 3 Logistic regression analysis of LVH and BP indexes in NT

	Model 1	Model 2	Model 3
24h SBP	1.052# (1.019–1.087)	1.061# (1.019–1.105)	1.057# (1.017–1.098)
24h PP	1.075# (1.038–1.113)	1.054* (1.008–1.103)	Not in
Daytime SBP	1.037* (1.007–1.067)	1.051# (1.013–1.090)	Not in
Daytime PP	1.067# (1.033–1.103)	1.050* (1.006–1.095)	
SD of daytime SBP	1.128# (1.040–1.225)	1.097 (.986–1.220)	
Nighttime SBP	1.041* (1.010–1.074)	1.027 (.995–1.060)	
Nighttime MAP	1.044 (0.995–1.095)	1.034 (.988–1.081)	
Nighttime PP	1.051# (1.016–1.087)	1.029 (.989–1.070)	
SD of nighttime SBP	1.094* (1.010–1.185)	1.117* (1.008–1.238)	Not in
Office SBP	1.024* (1.002–1.046)	1.012 (.986–1.038)	
Office PP	1.044# (1.020–1.068)	1.015 (.985–1.045)	
Office HR	.988 (.967–1.010)	.992 (.967–1.018)	
Nighttime DBP dip	.949# (.913–.986)	.975 (.925–1.028)	
Nighttime MAP dip	.945# (.906–.986)	.972 (.920–1.027)	

* represents $P < .05$, # represents $P < .01$.
Model 1: Univariate logistic regression analysis.
Model 2: Multivariate logistic regression analysis: 1 BP index + covariates including age, sex (male or female), smoking status (yes or no), drinking status (yes or no), BMI, FBG, CREA, URIC, TG, TC, HDL-C, and LDL-C.
Model 3: Multivariate forward logistic regression analysis: 24h SBP + 24h PP + Daytime SBP + SD of nighttime SBP + covariates used in Model 2 (Daytime PP was excluded after collinearity diagnostics).
Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; PP, pulse pressure; HR, heart rate.

TABLE 4 Logistic regression analysis of LVH and BP indexes in WCH

	Model 1	Model 2	Model 3
24h SBP	1.070* (1.010–1.134)	1.079* (1.001–1.164)	Not in
24h PP	1.068# (1.020–1.118)	1.022 (.957–1.091)	
Daytime SBP	1.044 (.992–1.100)	1.053 (.985–1.125)	
Daytime PP	1.056* (1.012–1.101)	1.010 (.952–1.072)	
SD of daytime SBP	1.136 (.995–1.296)	1.048 (.876–1.255)	
Nighttime SBP	1.070# (1.017–1.125)	1.072* (1.006–1.142)	Not in
Nighttime MAP	1.089* (1.001–1.185)	1.133* (1.021–1.257)	1.114* (1.005–1.235)
Nighttime PP	1.076# (1.025–1.130)	1.045 (.976–1.120)	
SD of nighttime SBP	.993 (.893–1.103)	.965 (.826–1.127)	
Office SBP	1.061# (1.022–1.101)	1.069* (1.016–1.126)	1.067# (1.019–1.117)
Office PP	1.044# (1.015–1.074)	1.026 (.985–1.068)	
Office HR	.970* (.944–.997)	.988 (.952–1.025)	
Nighttime DBP dip	.942 (.880–1.008)	.974 (.903–1.049)	
Nighttime MAP dip	.933 (.863–1.009)	.956 (.876–1.044)	

* represents $P < .05$, # represents $P < .01$.
Model 1: Univariate logistic regression analysis.
Model 2: Multivariate logistic regression analysis: 1 BP index + covariates including age, sex (male or female), smoking status (yes or no), drinking status (yes or no), BMI, FBG, CREA, URIC, TG, TC, HDL-C, and LDL-C.
Model 3: Multivariate forward logistic regression analysis: 24h SBP + Nighttime SBP + Nighttime MAP + Office SBP + covariates used in Model 2.
Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; PP, pulse pressure; HR, heart rate.

coworkers[10] conducted a case-control study comparing LVMI between WCH and normotensives, and found that LVMI was similar between the two groups. Nevertheless, more recent studies have shown that prognostically relevant target organ damages are more prevalent in WCH, compared with normotensives. The PAMELA study is one of the most widely acknowledged WCH studies, with a large cohort that underwent comprehensive blood pressure monitoring during a long follow-up period.[11] As demonstrated by the PAMELA study, LVMI and the prevalence of LVH were both significantly greater in WCH patients than those in normotensives,[1] which is consistent with the results of our study. A meta-analysis performed by Cuspidi and coworkers[12] also concluded that alterations in cardiac structure and function in ABPM-defined WCH were intermediate between sustained hypertensives and normotensive patients.

4.2 | Different factors associated with LVH in the two groups

To further determine what was associated with the occurrence of LVH in the two groups, we performed logistic regression analyses. We found that 24h SBP in the NT group and both nighttime MAP and office SBP in the WCH group could enter the final model in the forward logistic regression analysis, respectively, suggesting that influencing factors of LVH can be different in the two groups. Elevated average 24h BP has long been considered to be well related to hypertension target organ damage, based on both cross-sectional and longitudinal evidence.[13] To be noticed, from our results we can see that, in both the NT and WCH groups, 24h SBP was associated with LVH even when adjusted for baseline demographic and blood test data. However, when substituted into the forward logistic regression analysis together with other significant BP indexes in model 3, 24h SBP was still significantly associated with LVH in the NT group, while such relation was eliminated by nighttime MAP and office SBP in WCH participants. Therefore, we formed the hypothesis that nighttime BP and OBP may play more important roles in the onset and progression of LVH in the WCH population. Huang and coworkers[14] showed that the risk of WCH patients was higher than that of normotensive controls even after adjustment, suggesting the BP pattern in WCH patients also contributes to the process. This result was confirmed in our study.

Nighttime BP has previously been proved to be closely associated with target organ damages,[15] and shown to carry higher prognostic value in cardiovascular events than daytime BP or OBP.[16,17] Gijón and coworkers[18] reported that, compared with normotensive patients, mean nighttime SBP and DBP were significantly higher in WCH patients, which is consistent with our study. Bochud and coworkers[19] found that white-coat effect was inversely and independently associated with nighttime BP dipping. Cuspidi and coworkers[20] also showed that the prevalence of nocturnal hypertension was relatively high in the WCH population, which could increase cardiovascular risks in WCH patients. To be noted, though all the participants enrolled in our study had nighttime BP within 120/70 mm Hg, nighttime BP in the WCH population was higher than in the NT population. While this relatively elevated nighttime BP did not reach the diagnostic cut-off value, it could still be involved in the process of target organ damage in our WCH population. However, opposite opinion also existed. Maseko and coworkers[21] once reported that, in a group of African ancestry, nighttime SBP was not associated with LVMI and did not contribute to the relationship between white-coat effect and LVMI. Their results were drawn from participants including both normotensive and hypertensive populations, which could account for the differences from our study. Additionally, in our study, nighttime MAP rather than nighttime SBP was found to be more significantly associated with LVH, possibly because MAP contains risk-related information associated with both systolic and diastolic BP.[22] The clinical value of MAP cannot be neglected, as Melgarejo and coworkers[23] also showed that the use of 24h MAP, in conjunction with SBP and DBP, refined risk estimates.

OBP, the elevation of which is the main feature of WCH, has been widely applied in clinical settings and considered to be closely associated with cardiovascular risks.[24] Konstantinos and coworkers[25] showed that OBP was a predictor of aortic elastic properties and urinary protein excretion in WCH patients. Giuseppe and coworkers[26] also mentioned that persistently elevated OBP was prognostically relevant in WCH. Furthermore, OBP was identified as a predictor of new-onset sustained hypertension in the PAMELA study.[27] Our study also found that elevated office SBP was independently associated with the occurrence of LVH and, therefore, may play a role in target organ damage in WCH.

The pathogenetic mechanisms of WCH may underlie the different influencing factors observed between the two groups. Grassi and coworkers[28] once reported that, compared with normotensive patients, those with WCH had significantly greater resting sympathetic nerve activity values, possibly contributing to the increased target organ damage and cardiovascular risks seen in these patients. As the sympathetic nervous system plays an important role in the regulation of blood pressure, sympathetic dysfunction can manifest as elevated nighttime BP and attenuated nighttime dip.[29] Therefore, the more prominent relationship between nighttime BP and LVH seen in WCH patients, compared with the NT group, may be partly due to abnormal sympathetic activity. Elevated office SBP in WCH individuals has been associated with activation of the sympathetic nervous system too.[30] Moreover, a temporal stress response in the clinical environment where office SBP is measured may reflect inherent hyper-reactivity to stress, which can be harmful in the long-term.[31]

4.3 | Limitations

First, as a cross-sectional study conducted in one hospital, selection bias was inevitable in our study, resulting in a higher proportion of WCH and fewer normotensive patients who underwent ABPM and were enrolled in our study. Therefore, a large prospective longitudinal study performed in a general population is further needed to confirm our conclusions. Second, WCH was diagnosed by OBP acquired in one clinic visit, which may lead to false positives in WCH due to the repeatability of OBP. Subsequent follow-up is warranted to identify whether

there is still a relationship between WCH and LVH if WCH diagnosis is based on serial OBP measurements. Third, the detailed mechanism by which nighttime and office BP affect the left ventricle cannot be determined in our study, since it was cross-sectional and lacked the study design to answer this question.

5 | CONCLUSIONS

In conclusions, when WCH was defined as elevated office BP but normal ABPM in all 24h, daytime and nighttime periods, the proportion of LVH observed in our study was higher in WCH than in NT. The BP indexes associated with LVH varied between the two groups. 24h SBP was correlated with LVH in the NT population, while relatively elevated nighttime MAP and office SBP were associated with LVH in WCH patients.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

AUTHOR CONTRIBUTIONS

Dr. Chen has full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. All co-authors have reviewed and approved of the manuscript prior to submission. Xiangyu Yang and Yuan Yuan make equal contributions to this work. Study concept and design: Xiangyu Yang, Yuan Yuan, Xiaoping Chen. Acquisition of data: Xiangyu Yang, Yuan Yuan, Jiangbo Li, Jun Ma, Yanan Li. Analysis and interpretation of data: Xiangyu Yang, Yuan Yuan, Qiling Gou, Runyu Ye, Xinran Li, Xiaoping Chen. Drafting of the manuscript: Xiangyu Yang, Yuan Yuan, Xiaoping Chen. Critical revision of the manuscript for important intellectual content: Qiling Gou, Jiangbo Li, Xiaoping Chen. Study supervision: Xiangyu Yang, Xiaoping Chen.

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REFERENCES

1. Sega R, Trocino G, Lanzarotti A, et al. Alterations of cardiac structure in patients with isolated office, ambulatory, or home hypertension: data from the general population (Pressione Arteriose Monitorate E Loro Associazioni [PAMELA] Study). *Circulation*. 2001;104(12):1385-1392.
2. Mancia G, Facchetti R, Bombelli M, Cuspidi C, Grassi G. White-coat hypertension: pathophysiological and clinical aspects: excellence award for hypertension research 2020. *Hypertension*. 2021;78(6):1677-1688.
3. Mancia G, De Backer G, Dominiczak A, et al. 2007 Guidelines for the Management of Arterial Hypertension: the Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *J Hypertens*. 2007;25(6):1105-1187.
4. O'Brien E, Parati G, Stergiou G, et al. European Society of Hypertension position paper on ambulatory blood pressure monitoring. *J Hypertens*. 2013;31(9):1731-1768.
5. de la SierraA, Segura J, Banegas JR, et al. Clinical features of 8295 patients with resistant hypertension classified on the basis of ambulatory blood pressure monitoring. *Hypertension*. 2011;57(5):898-902.
6. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Hypertension*. 2018;71(6):e13-e115.
7. Omboni S. A working definition of white-coat hypertension must include nocturnal blood pressure. *J Clin Hypertens (Greenwich)*. 2018;20(8):1183-1186.
8. Mancia G, Fagard R, Narkiewicz K, et al. 2013 ESH/ESC guidelines for the management of arterial hypertension: the Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *J Hypertens*. 2013;31(7):1281-1357.
9. Pickering TG, James GD, Boddie C, Harshfield GA, Blank S, Laragh JH. How common is white coat hypertension?. *Jama*. 1988;259(2):225-228.
10. Cavallini MC, Roman MJ, Pickering TG, Schwartz JE, Pini R, Devereux RB. Is white coat hypertension associated with arterial disease or left ventricular hypertrophy?. *Hypertension*. 1995;26(3):413-419.
11. Bombelli M, Toso E, Peronio M, et al. The Pamela study: main findings and perspectives. *Curr Hypertens Rep*. 2013;15(3):238-243.
12. Cuspidi C, Rescaldani M, Tadic M, Sala C, Grassi G, Mancia G. White-coat hypertension, as defined by ambulatory blood pressure monitoring, and subclinical cardiac organ damage: a meta-analysis. *J Hypertens*. 2015;33(1):24-32.
13. Mancia G, Parati G. Ambulatory blood pressure monitoring and organ damage. *Hypertension*. 2000;36(5):894-900.
14. Huang Y, Huang W, Mai W, et al. White-coat hypertension is a risk factor for cardiovascular diseases and total mortality. *J Hypertens*. 2017;35(4):677-688.
15. O'Flynn AM, Dolan E, Curtin RJ, O'Brien E, Perry IJ, Kearney PM. Night-time blood pressure and target organ damage: a comparative analysis of absolute blood pressure and dipping status. *J Hypertens*. 2015;33(11):2257-2264.
16. Hansen TW, Li Y, Boggia J, Thijs L, Richart T, Staessen JA. Predictive role of the nighttime blood pressure. *Hypertension*. 2011;57(1):3-10.
17. Roush GC, Fagard RH, Salles GF, et al. Prognostic impact from clinic, daytime, and night-time systolic blood pressure in nine cohorts of 13,844 patients with hypertension. *J Hypertens*. 2014;32(12):2332-2340.
18. Gijón-Conde T, Graciani A, López-García E, et al. Short-term variability and nocturnal decline in ambulatory blood pressure in normotension, white-coat hypertension, masked hypertension and sustained hypertension: a population-based study of older individuals in Spain. *Hypertens Res*. 2017;40(6):613-619.
19. Bochud M, Bovet P, Vollenweider P, et al. Association between white-coat effect and blunted dipping of nocturnal blood pressure. *Am J Hypertens*. 2009;22(10):1054-1061.
20. Cuspidi C, Paoletti F, Tadic M, et al. Nocturnal blood pressure: the dark side of white-coat hypertension. *J Hypertens*. 2020;38(12):2404-2408.
21. Maseko MJ, Woodiwiss AJ, Libhaber CD, Brooksbank R, Majane OH, Norton GR. Relations between white coat effects and left ventricular mass index or arterial stiffness: role of nocturnal blood pressure dipping. *Am J Hypertens*. 2013;26(11):1287-1294.

22. Flint AC, Conell C, Ren X, et al. Effect of systolic and diastolic blood pressure on cardiovascular outcomes. *N Engl J Med*. 2019;381(3):243-251.
23. Melgarejo JD, Yang WY, Thijs L, et al. Association of fatal and non-fatal cardiovascular outcomes with 24-hour mean arterial pressure. *Hypertension*. 2021;77(1):39-48.
24. Cohn JN, Duprez DA, Hoke L, Florea N, Duval S. Office blood pressure and cardiovascular disease: pathophysiologic implications for diagnosis and treatment. *Hypertension*. 2017;69(5):e14-e20.
25. Aznaouridis K, Vlachopoulos C, Masoura K, et al. Office blood pressure is a predictor of aortic elastic properties and urinary protein excretion in subjects with white coat hypertension. *Int J Cardiol*. 2016;203:98-103.
26. Mancia G, Facchetti R, Grassi G, Bombelli M. Adverse prognostic value of persistent office blood pressure elevation in white coat hypertension. *Hypertension*. 2015;66(2):437-444.
27. Mancia G, Bombelli M, Brambilla G, et al. Long-term prognostic value of white coat hypertension: an insight from diagnostic use of both ambulatory and home blood pressure measurements. *Hypertension*. 2013;62(1):168-174.
28. Grassi G, Seravalle G, Trevano FQ, et al. Neurogenic abnormalities in masked hypertension. *Hypertension*. 2007;50(3):537-542.
29. Sherwood A, Steffen PR, Blumenthal JA, Kuhn C, Hinderliter AL. Nighttime blood pressure dipping: the role of the sympathetic nervous system. *Am J Hypertens*. 2002;15(2 Pt 1)):111-118.
30. Grassi G, Turri C, Vailati S, Dell'Oro R, Mancia G. Muscle and skin sympathetic nerve traffic during the "white-coat" effect. *Circulation*. 1999;100(3):222-225.
31. Munakata M. Clinical significance of stress-related increase in blood pressure: current evidence in office and out-of-office settings. *Hypertens Res*. 2018;41(8):553-569.

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