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ARTICLE

Impact of hypertension phenotypes on the office and 24-h pulse wave velocity and augmentation index in individuals with or without antihypertensive medication use

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Abstract

Data on the association of blood pressure (BP) phenotypes with office and out-of-office markers of vascular stiffness and pressure wave reflection are sparse. This study investigated office and 24-h measures of brachial BP, pulse wave velocity (PWV), and central augmentation index (AIx) across hypertension phenotypes among individuals not using BP-lowering medications [normotension (NT), white-coat hypertension (WH), masked hypertension (MH) and sustained hypertension (SH)] and those using BP-lowering medications [controlled hypertension (CH), white-coat uncontrolled hypertension (WUCH), masked uncontrolled hypertension (MUCH) and sustained uncontrolled hypertension (SUCH)]. We evaluated 454 untreated (age = 45 ± 15 years, 50% males) and 238 treated (age = 52 ± 15 years, 45% males) individuals who underwent office and 24-h brachial BP, PWV, and AIx measures using a Mobil-O-Graph PWA monitor. In the analysis adjusted for age and sex, WH had higher ($p < 0.05$) office PWV (7.53 ± 0.09 vs 6.89 ± 0.05), office AIx (27.9 ± 1.3 vs 23.8 ± 0.8), and daytime AIx (24.6 ± 0.7 vs 22.7 ± 0.4) compared with those of NT, while WUCH had higher ($p < 0.05$) office PWV (8.28 ± 0.11 vs 7.43 ± 0.08) and 24-h PWV (7.54 ± 0.09 vs 7.21 ± 0.07) than those of CH. MH had higher ($p < 0.05$) 24-h PWV (7.00 ± 0.09 vs 6.69 ± 0.04) and 24-h AIx (24.3 ± 0.9 vs 21.9 ± 0.4) than those of NT, whereas MUCH had higher ($p < 0.05$) 24-h PWV (7.64 ± 0.13 vs 7.21 ± 0.07) than that of CH. Lastly, SH or SUCH had significantly higher office and 24-h PWV and AIx than those of NT and CH, respectively. In conclusion, these results suggest that individuals with masked BP phenotypes are more predisposed to have adverse out-of-office vascular characteristics, while individuals with white-coat phenotypes have adverse office and out-of-office vascular characteristics compared with those of individuals with normal BP levels.

Keywords Arterial stiffness · Masked hypertension · White-coat hypertension · Ambulatory blood pressure monitoring

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Introduction

Elevated blood pressure is a major modifiable risk factor for cardiovascular events [1, 2]. In clinical practice, blood pressure (BP) is usually evaluated in the office, but this approach may underestimate or overestimate true BP levels. Therefore, assessment of ambulatory or home BP has been encouraged by current BP guidelines to determine the presence of white-coat and masked BP phenomena and to identify clinically relevant phenotypes, such as white-coat hypertension (WH) and masked hypertension (MH) in individuals not using BP-lowering medications, and white-coat uncontrolled hypertension (WUCH), and masked uncontrolled hypertension (MUCH) in individuals using BP-lowering medications [3–5].

Several clinical and epidemiological studies have shown that MH and MUCH have poorer prognoses and greater cardiovascular damage when compared with those of normotension (NT) and controlled hypertension (CH), respectively [6, 7]. In contrast, whether individuals with white-coat phenotypes have a worse prognosis remains a controversial issue, since similar and higher long-term risks have been reported for this population in comparison with the risk in individuals with normal BP values [6, 8–10].

Novel devices have allowed the joint evaluation of office and 24-h BP and markers of vascular stiffness and pressure wave reflection, including pulse wave velocity (PWV) and the central augmentation index (AIx), respectively, which may improve the estimation of vascular damage and risk [11–14]. However, knowledge regarding the impact of hypertension phenotypes on out-of-office measures of vascular stiffness and pressure wave reflection is sparse [13, 14]. This study aimed to investigate office and 24-h measures of BP, PWV, and AIx across the hypertension phenotypes of individuals not using BP-lowering medications [NT, WH, MH, and sustained hypertension (SH)] and those using BP-lowering medications [CH, WUCH, MUCH, and sustained uncontrolled hypertension (SUCH)].

Methods

Study population

This cross-sectional observational study evaluated 692 subjects (454 not using and 238 using BP-lowering medications), with age > 18 years, enrolled from the Clinical Research Center of the Cesmac University Center from 2014 to 2016. All participants underwent measures of office and ambulatory brachial BP, PWV, and AIx. The study protocol conforms to the principles of the Declaration of Helsinki and was approved by The Ethics committee of the Pedro Ernesto University Hospital. All participants provided written informed consent.

Office and ambulatory BP, PWV, and AIx measures

Office and 24-h brachial systolic BP (SBP) and diastolic BP (DBP), PWV, and AIx measures were obtained using a Mobil-O-Graph PWA monitor (IEM Healthcare, Stolberg, Germany), as previously reported [13, 15, 16]. This device allows oscillometric recognition of the peripheral pulse wave and constructs the central pulse wave using an inbuilt algorithm (ARCSolver). PWV measurements were calculated from the difference in time between the estimated forward and reflected waves and are similar to intra-aortic catheter measurements [17]. AIx measurements were estimated as the augmentation pressure to pulse pressure ratio and are similar to those acquired by a widely used non-invasive method (Sphygmocor system) [18]. In addition, the Mobil-O-Graph PWA monitor has good feasibility and reproducibility for assessing ambulatory PWV and AIx measurements [19, 20].

Three office brachial BP, PWV, and AIx readings were taken after 5 min of rest in the sitting position, and their means were considered office measures. Ambulatory measures of brachial BP, PWV, and AIx comprised 24-h readings obtained at 30-min intervals. For the current analysis, we only included subjects with at least 16 and 8 valid daytime and nighttime readings, respectively. Mean arterial pressure was estimated as SBP/3 + 2*DBP/3.

Hypertension phenotypes and clinical characteristics

Hypertension phenotypes among subjects not using BP-lowering medications were defined as follows: NT (office SBP < 140 mmHg and DBP < 90 mmHg and 24-h SBP < 130 mmHg and DBP < 80 mmHg), WH (office SBP ≥ 140 mmHg or DBP ≥ 90 mmHg and 24-h SBP < 130 mmHg and DBP < 80 mmHg), MH (office SBP < 140 mmHg and DBP < 90 mmHg and 24-h SBP ≥ 130 mmHg or DBP ≥ 80 mmHg), and SH (office SBP ≥ 140 or DBP ≥ 90 mmHg and 24-h SBP ≥ 130 or DBP ≥ 80 mmHg) [4]. The corresponding terminologies were used among participants using BP-lowering medications: CH, WUCH, MUCH, and SUCH.

Data on age, sex, body mass index, use of antidiabetic and lipid-lowering medications, and current smoking were obtained from all participants. All participants were also actively asked regarding their performance of physical activity, and those who stated that they regularly performed physical activity (e.g., walking, jogging, running, cycling, training at the gym, and performing sports) at least 3 days a week were considered physically active.

Statistical analysis

Continuous data are presented as the mean ± standard deviation, while categorical variables are presented as proportions. Comparisons of continuous variables among the studied groups were performed using one-way ANOVA followed by the Bonferroni's test, while comparisons of categorical variables were performed using the Bonferroni-corrected chi-square test. PWV and AIx measures were also presented as the multivariable adjusted mean ± standard error (considering age and sex as adjusting variables) from linear regression models across hypertension phenotypes. To further evaluate the impact of BP on the relationship between vascular parameters and the studied groups, we performed multivariable analysis adjusted for age, sex, and mean arterial pressure. P-values < 0.05 were considered significant. Statistical analysis was performed using Stata

Table 1 Clinical and blood pressure characteristics of participants not using blood pressure-lowering lowering medications

	NT ($n = 194$)	WH ($n = 68$)	MH ($n = 38$)	SH ($n = 154$)
Male sex, *n* (%)	86 (44)	36 (53)	22 (58)	85 (55)
Age, years	42.2 ± 15.6	45.7 ± 16.7	46.8 ± 15.2	47.1 ± 14.5*
Body mass index, k/m^2	27.0 ± 4.2	27.6 ± 4.3	27.5 ± 3.3	28.8 ± 11.4
Hypolipemiant med, *n* (%)	7 (4)	4 (6)	2 (5)	7 (5)
Antidiabetic med, *n* (%)	8 (4)	3 (4)	0 (0)	8 (5)
Physical activity, *n* (%)	63 (33)	26 (38)	12 (32)	43 (28)
Current smoking, *n* (%)	2 (1)	0 (0)	1 (3)	6 (4)
Office SBP, mmHg	120.8 ± 10.3	140.2 ± 12.4*	124.7 ± 10.2†	144.5 ± 16.9*‡
Office DBP, mmHg	77.4 ± 7.6	89.5 ± 8.9*	82.4 ± 7.4*†	98.1 ± 10.9*†‡
Office MAP, mmHg	91.9 ± 7.1	106.4 ± 6.0*	96.5 ± 7.5*†	113.6 ± 10.3*†‡
24 h SBP, mmHg	113.5 ± 7.7	118.0 ± 6.1*	126.9 ± 9.2*†	129.7 ± 9.6*†
24 h DBP, mmHg	70.3 ± 5.9	73.6 ± 4.4*	82.1 ± 5.4*†	85.8 ± 6.8*†‡
24 h MAP, mmHg	84.7 ± 5.6	88.4 ± 3.6*	97.1 ± 5.0*†	100.4 ± 6.6*†‡
Daytime SBP, mmHg	116.3 ± 7.8	121.1 ± 7.4*	130.0 ± 8.8*†	133.0 ± 9.3*†
Daytime DBP, mmHg	73.3 ± 6.5	76.4 ± 5.3*	84.9 ± 6.6*†	89.1 ± 7.6*†‡
Daytime MAP, mmHg	87.6 ± 6.0	91.3 ± 4.8*	99.9 ± 5.6*†	103.7 ± 7.0*†‡
Nighttime SBP, mmHg	108.9 ± 9.2	113.0 ± 7.4	121.2 ± 12.1*†	123.2 ± 15.2*†
Nighttime DBP, mmHg	65.2 ± 6.8	69.1 ± 5.3*	77.1 ± 6.3*†	79.9 ± 8.6*†
Nighttime MAP, mmHg	79.8 ± 6.8	83.7 ± 4.9*	91.8 ± 7.2*†	94.3 ± 9.5*†

DBP diastolic blood pressure, *SBP* systolic blood pressure, *MAP* mean arterial pressure, *med* medications, *NT* normotension, *WH* white-coat hypertension, *MH* masked hypertension, *SH* sustained hypertension

*$P < 0.05$ compared with NT; $^{\dagger}P < 0.05$ compared with WH; $^{\ddagger}P < 0.05$ compared with MH

software Version 14.1 (Stata Corp LP, College Station, TX, USA).

Results

Clinical characteristics and BP measures of participants untreated and treated with antihypertensive medications

Clinical characteristics and BP measures of participants not using BP-lowering medications ($n = 454$, mean age = 45 ± 15 years, 50% males) are shown in Table 1. There were 43%, 15%, 8%, and 34% with NT, WH, MH, and SH, respectively. SH had a higher age than that of NT, while the studied groups had a similar sex distribution, body mass index, and prevalence of physical activity. The prevalence of current smokers and the use of lipid-lowering and antidiabetic medications were low (at least ≤ 5% within each group) and similar among the studied groups. NT had lower office and ambulatory SBP and DBP measures compared with those of all the other groups. SH had higher BP measures compared with the other groups, except for office SBP, which was similar to those of WH, and ambulatory SBP and nighttime DBP measures, which were similar to those of MH. As expected, WH had higher office BP measures and lower ambulatory BP measures than did MH.

Among participants using BP-lowering medications ($n = 238$, mean age = 52 ± 15 years, 45% males), there were 31%, 19%, 9%, and 41% with CH, WUCH, MUCH, and SUCH, respectively (Table 2). Age, sex distribution, body mass index, prevalence of current smokers and physical activity, and the use of lipid-lowering and antidiabetic medications were similar among the studied groups. In general, CH had the lowest office and ambulatory BP measures, while SUCH had the highest office and ambulatory BP measures among the studied groups. In addition, WUCH had higher office BP but lower ambulatory BP levels compared with those of MUCH.

Vascular characteristics of participants untreated and treated with antihypertensive medications

The vascular characteristics of participants not using BP-lowering medications according to hypertension phenotypes are shown in Table 3. In the analysis adjusted for age and sex, WH and SH showed the highest office PWV and AIx values, while MH and SH had the highest ambulatory PWV and 24-h AIx values among the studied groups. In addition, WH had a higher daytime AIx compared with that of NT. Conversely, in the analysis further adjusted for mean arterial

Table 2 Clinical and blood pressure characteristics of participants using blood pressure-lowering medications

	CH ($n = 74$)	WUCH ($n = 44$)	MUCH ($n = 22$)	SUCH ($n = 98$)
Male sex, *n* (%)	25 (34)	13 (30)	15 (68)	55 (56)
Age, years	53.6 ± 13.3	54.9 ± 15.2	46.1 ± 13.8	49.9 ± 14.1
Body mass index, k/m^2	27.7 ± 3.9	28.1 ± 4.9	28.1 ± 3.7	27.8 ± 5.0
Hypolipemiant med, *n* (%)	26 (35)	13 (30)	4 (18)	22 (22)
Antidiabetic med, *n* (%)	9 (12)	6 (14)	1 (5)	12 (12)
Physical activity, *n* (%)	26 (35)	13 (30)	6 (27)	26 (27)
Current smoking, *n* (%)	1 (1)	2 (5)	0 (0)	3 (3)
Office SBP, mmHg	121.8 ± 9.8	143.1 ± 16.0*	121.5 ± 12.2†	148.8 ± 15.0*‡
Office DBP, mmHg	78.7 ± 7.6	91.0 ± 10.7*	79.3 ± 9.2†	101.4 ± 11.9*†‡
Office MAP, mmHg	93.1 ± 7.3	108.4 ± 9.0*	93.4 ± 9.1*†	117.2 ± 11.3*†‡
24 h SBP, mmHg	113.9 ± 6.6	118.7 ± 7.0*	123.3 ± 6.5*	133.4 ± 11.1*†‡
24 h DBP, mmHg	70.0 ± 6.2	72.6 ± 5.1	81.2 ± 4.3*†	88.0 ± 8.2*†‡
24 h MAP, mmHg	84.6 ± 5.4	87.9 ± 4.5*	95.2 ± 3.0*†	103.1 ± 8.0*†‡
Daytime SBP, mmHg	116.0 ± 7.3	121.2 ± 8.2*	125.0 ± 6.8*	136.2 ± 10.7*†‡
Daytime DBP, mmHg	72.5 ± 7.0	74.8 ± 5.3	83.4 ± 4.2*†	90.9 ± 8.4*†‡
Daytime MAP, mmHg	87.0 ± 6.2	90.3 ± 5.1	97.2 ± 3.1*†	106.0 ± 8.1*†‡
Nighttime SBP, mmHg	110.4 ± 8.4	114.0 ± 8.3	120.7 ± 8.1*	127.7 ± 17.8*†
Nighttime DBP, mmHg	66.1 ± 6.5	68.6 ± 6.7	77.1 ± 6.5*†	82.9 ± 10.0*†‡
Nighttime MAP, mmHg	80.8 ± 6.4	83.7 ± 6.1	91.7 ± 5.6*†	97.8 ± 11.1*†‡

DBP diastolic blood pressure, *SBP* systolic blood pressure, *MAP* mean arterial pressure, *med* medications, *CH* controlled hypertension, *WUCH* white-coat uncontrolled hypertension, *MUCH* masked uncontrolled hypertension, *SUCH* sustained uncontrolled hypertension

*$P < 0.05$ compared with CH; $^{\dagger}P < 0.05$ compared with WUCH; $^{\ddagger}P < 0.05$ compared with MUCH

pressure, NT did not have lower values of PWV and AIx in comparison with those of the other hypertension phenotypes (Table 3).

In the analysis adjusted for age and sex among participants using BP-lowering medications, those with WUCH and SUCH had similar office PWV values, which were higher than those with MUCH and CH (Table 4). WUCH and MUCH had similar ambulatory PWV values, which were higher than the value of CH but lower than that of SUCH. In contrast, MUCH and SUCH tended to show the highest numerical office and AIx ambulatory values among the studied groups. In further analyses adjusted for mean arterial pressure, WUCH and SUCH still had higher values of office and out-of-office PWV compared with those of CH, while MUCH had the highest office AIx values among the studied groups (Table 4).

Discussion

The present study evaluated the impact of hypertension phenotypes on office and 24-h BP, PWV, and AIx in individuals untreated or treated with antihypertensive medications. In the analysis adjusted for age and sex, WH had higher office PWV and AIx and daytime AIx compared with the values of NT, while WUCH had higher office and ambulatory 24-h PWV than those of CH. Conversely, MH had higher ambulatory PWV and AIx than did NT, whereas MUCH had higher ambulatory PWV than that of CH. In addition, SH or SUCH had higher office and ambulatory PWV and Aix than those of NT and CH, respectively. In general, these results suggest that individuals with masked BP phenotypes are more predisposed to have adverse out-of-office vascular characteristics, while individuals with white-coat BP phenotypes have adverse office and out-of-office vascular characteristics compared with those of individuals with normal BP levels. These findings might contribute to explaining the adverse outcomes reported for individuals with white-coat and masked BP elevation [6–8, 21].

Although some studies have not provided a consistent association [9, 10], alternative epidemiological evidence has suggested that white-coat BP elevation has worse long-term outcomes compared with normal office and out-of-office BP levels [6, 8, 21]. However, the mechanisms underlying the higher cardiovascular risk related to white-coat BP phenomena are not well elucidated. In our analysis adjusted for age and sex, WH had higher office PWV and AIx than those of NT, which agrees with evidence obtained in other populations [22, 23] and supports the notion that WH is coupled with adverse vascular characteristics. On the other

Table 3 Vascular parameters among participants not using blood pressure-lowering medications

	Unadjusted				Adjusted for age and sex				Adjusted for age, sex and, mean arterial pressure[a]			
	NT ($n = 194$)	WH ($n = 68$)	MH ($n = 38$)	SH (n = 154)	NT ($n = 194$)	WH ($n = 68$)	MH ($n = 38$)	SH ($n = 154$)	NT ($n = 194$)	WH ($n = 68$)	MH ($n = 38$)	SH ($n = 154$)
Office PWV, m/s	6.60 ± 1.69	7.63 ± 2.03*	7.12 ± 1.89	7.80 ± 1.89*	6.89 ± 0.05	7.53 ± 0.09*	6.90 ± 0.12†	7.54 ± 0.06*‡	7.31 ± 0.06	7.34 ± 0.08	7.12 ± 0.10	7.05 ± 0.07*†
24 h PWV, m/s	6.40 ± 1.64	6.90 ± 1.90	7.22 ± 1.98*	7.35 ± 1.74*	6.69 ± 0.04	6.80 ± 0.07	7.00 ± 0.09*	7.09 ± 0.05*†	6.94 ± 0.05	6.92 ± 0.07	6.81 ± 0.09	6.77 ± 0.06
Daytime PWV, m/s	6.47 ± 1.63	6.99 ± 1.88	7.29 ± 1.94*	7.44 ± 1.70*	6.75 ± 0.04	6.89 ± 0.07	7.07 ± 0.09*	7.19 ± 0.05*†	6.99 ± 0.05	7.00 ± 0.06	6.90 ± 0.09	6.89 ± 0.06
Nighttime PWV, m/s	6.29 ± 1.67	6.78 ± 1.95	7.09 ± 2.09	7.18 ± 1.84	6.58 ± 0.05	6.68 ± 0.07	6.87 ± 0.10*	6.92 ± 0.05*†	6.79 ± 0.05	6.77 ± 0.07	6.69 ± 0.10	6.66 ± 0.05
Office AIx	24.1 ± 11.7	27.7 ± 10.7	25.2 ± 11.5	27.4 ± 11.6*	23.8 ± 0.8	27.9 ± 1.3*	25.7 ± 1.7	27.6 ± 0.8*	25.2 ± 1.0	27.2 ± 1.3	26.5 ± 1.7	25.9 ± 1.1
24 h AIx	22.1 ± 8.7	22.9 ± 8.9	23.9 ± 8.1	25.1 ± 8.7*	21.9 ± 0.4	23.0 ± 0.7	24.3 ± 0.9*	25.2 ± 0.5*†	23.4 ± 0.5	23.7 ± 0.7	23.1 ± 1.0	23.2 ± 0.6
Daytime AIx	23.1 ± 8.5	24.4 ± 8.4	25.4 ± 7.3	26.7 ± 8.4*	22.7 ± 0.4	24.6 ± 0.7*	26.0 ± 1.0*	26.9 ± 0.5*†	24.2 ± 0.5	25.2 ± 0.7	24.9 ± 1.0	25.1 ± 0.6
Nighttime AIx	20.7 ± 11.2	20.8 ± 11.9	21.2 ± 10.6	22.3 ± 10.6	20.8 ± 0.6	20.8 ± 1.0	21.3 ± 1.3	22.1 ± 0.6	22.0 ± 0.6	21.3 ± 1.0	20.4 ± 1.3	20.7 ± 0.7

Unadjusted data are presented as mean ± standard deviation, while adjusted data are presented as mean ± standard error

PWV pulse wave velocity, *AIx* augmentation index, *NT* normotension, *WH* white-coat hypertension, *MH* masked hypertension, *SH* – sustained hypertension

*$P < 0.05$ compared with NT; $^{\dagger}P < 0.05$ compared with WH; $^{\ddagger}P < 0.05$ compared with MH

[a]Office, 24 h, daytime or nighttime mean arterial pressure values were used as covariates in the models for office, 24 h, daytime or nighttime vascular parameters, respectively

Table 4 Vascular parameters among participants using blood pressure-lowering medications

	Unadjusted				Adjusted for age and sex				Adjusted for age, sex and, mean arterial pressure[a]			
	CH ($n = 74$)	WUCH ($n = 44$)	MUCH ($n = 22$)	SUCH ($n = 98$)	CH ($n = 74$)	WUCH ($n = 44$)	MUCH ($n = 22$)	SUCH ($n = 98$)	CH ($n = 74$)	WUCH ($n = 44$)	MUCH ($n = 22$)	SUCH ($n = 98$)
Office PWV, m/s	7.68 ± 1.71	8.70 ± 2.32*	6.92 ± 1.37†	8.21 ± 1.84*	7.43 ± 0.08	8.28 ± 0.11*	7.61 ± 0.15†	8.43 ± 0.07*‡	7.81 ± 0.09	8.19 ± 0.10*	8.02 ± 0.15	8.10 ± 0.08*
24 h PWV, m/s	7.45 ± 1.70	7.94 ± 2.09	7.00 ± 1.38	7.72 ± 1.70	7.21 ± 0.07	7.54 ± 0.09*	7.64 ± 0.13*	7.93 ± 0.06*†‡	7.45 ± 0.08	7.69 ± 0.09*	7.63 ± 0.12	7.69 ± 0.08
Daytime PWV, m/s	7.50 ± 1.65	7.99 ± 2.06	7.01 ± 1.35	7.80 ± 1.69	7.26 ± 0.07	7.60 ± 0.09*	7.65 ± 0.12*	8.01 ± 0.06*†‡	7.47 ± 0.08	7.73 ± 0.09*	7.66 ± 0.12	7.79 ± 0.08*
Nighttime PWV, m/s	7.37 ± 1.77	7.79 ± 2.12	6.94 ± 1.43	7.59 ± 1.74	7.13 ± 0.08	7.39 ± 0.10*	7.60 ± 0.14*	7.81 ± 0.07*†	7.38 ± 0.08	7.55 ± 0.10	7.54 ± 0.13	7.56 ± 0.07
Office AIx	27.9 ± 11.5	28.4 ± 13.6	30.1 ± 9.2	28.4 ± 10.4	26.7 ± 1.2	26.7 ± 1.6	32.6 ± 2.2*†	29.5 ± 1.1	28.9 ± 1.5	26.1 ± 1.6	35.0 ± 2.4*†‡	27.6 ± 1.3
24 h AIx	26.1 ± 8.3	26.1 ± 9.0	23.5 ± 6.4	26.0 ± 9.0	24.5 ± 0.7	23.8 ± 0.9	27.0 ± 1.3	27.5 ± 0.6*†	26.0 ± 0.9	24.7 ± 1.0	26.9 ± 1.3	26.0 ± 0.9
Daytime AIx	26.2 ± 7.6	26.1 ± 8.4	24.3 ± 6.2	27.1 ± 8.4	24.9 ± 0.7	24.1 ± 0.9	27.2 ± 1.3	28.3 ± 0.6*†	26.3 ± 0.9	25.0 ± 1.0	27.2 ± 1.3	26.8 ± 0.8
Nighttime AIx	26.0 ± 11.6	26.6 ± 10.6	22.7 ± 10.3	24.1 ± 11.6	23.9 ± 1.0	23.7 ± 1.3	27.1 ± 1.9	25.9 ± 0.9	25.5 ± 1.1	24.7 ± 1.3	26.8 ± 1.8	24.4 ± 1.0

Unadjusted data are presented as mean ± standard deviation, while adjusted data are presented as mean ± standard error

PWV pulse wave velocity, *AIx* augmentation index, *CH* controlled hypertension, *WUCH* white-coat uncontrolled hypertension, *MUCH* masked uncontrolled hypertension, *SUCH* sustained uncontrolled hypertension

*$P < 0.05$ compared with CH; $^{\dagger}P < 0.05$ compared with WUCH; $^{\ddagger}P < 0.05$ compared with MUCH

[a]Office, 24 h, daytime or nighttime mean arterial pressure values were used as covariates in the models for office, 24 h, daytime or nighttime vascular parameters, respectively

hand, analysis of ambulatory measures of PWV and AIx revealed that WH only had greater daytime AIx compared with that of NT. These latter results suggest that WH might be associated with a limited impact on ambulatory markers of arterial stiffness among individuals not using BP-lowering medication. By contrast, when analyzing the sample using BP-lowering medications, we observed that WUCH had higher office and out-of-office PWV than the PWVs of CH. In addition to confirming that WUCH has greater office PWV [22], our data provide novel evidence that ambulatory measures of PWV are also abnormal in WUCH, reinforcing the idea that there is consistent vascular damage in this hypertension phenotype. This latter finding contrasts with a recent study performed in treated patients with chronic kidney disease, which did not observe differences in ambulatory 24-h PWV measures between WUCH and CH [13]. The reasons for these discrepancies are not clear, but the lower age in our sample and differences in clinical characteristics and sample size between the studied populations might have played a role in this regard.

In the present report, MH and MUCH had higher ambulatory PWV measures when compared with measures for NT and CH, respectively, in the analysis adjusted for age and sex. These findings strengthen the notion that a masked BP phenotype is associated with increased vascular damage and therefore adverse long-term outcomes [6, 7]. Furthermore, they agree with data from a mixed sample of South African individuals using and not using BP-lowering medications [14] and patients with chronic kidney disease [13], which showed higher 24-h, daytime and nighttime values of PWV among individuals with masked BP phenotype. Interestingly, consistent with previous evidence [24, 25], we found that office PWV did not differ between individuals with a masked BP phenotype and those with normal office and ambulatory BP levels, suggesting that ambulatory rather than office PWV measures might be more representative of vascular damage in individuals with a masked BP phenotype. In addition, 24-h, daytime and nighttime AIx values were not influenced by the masked BP phenotype, which indicates that the PWV and AIx might not share similar clinical value among individuals with MH or MUCH.

Some aspects of the current report deserve further comments. First, we found that SH and SUCH had higher office and ambulatory PWV and AIx than those of NT and CH, respectively, confirming that sustained higher BP levels are related to adverse vascular characteristics not only in the office but also out of the office [13, 14, 23, 26]. In addition, office PWV and AIx tended to be similar between white-coat and sustained elevated BP phenotypes, while ambulatory PWV and AIx values of masked and sustained elevated BP phenotypes were more comparable in the analysis adjusted for age and sex. Therefore, markers or vascular stiffness appear to reproduce the office and out-of-office BP variation patterns of hypertension phenotypes. Second, the analysis with further adjustment for mean arterial pressure showed no greater values of PWV or AIx in WH, MH, or SH compared with values in NT, indicating that vascular differences among the studied groups of untreated participants were largely related to the corresponding BP differences. In contrast, WUCH and SUCH still had greater office and out-of-office PWV than CH after adjusting for mean arterial pressure, suggesting that adverse vascular characteristics in treated participants with WUCH or SUCH might not be solely related to differences in BP values among the studied groups. Third, the prevalence rates of WH and WUCH were 15% and 19%, respectively, while the frequencies of WH and WUCH were in the range of 8% and 9%, respectively. These rates are similar to those recently reported for large alternative Brazilian populations evaluated by home blood pressure monitoring [27, 28], and might therefore be suggestive of the prevalence of white-coat and masked BP phenotypes in Brazil.

This study has some limitations. The cross-sectional nature of the protocol limits the ability to infer a causal relationship between hypertension phenotypes and markers of vascular stiffness and pressure wave reflection. Data on relevant covariates, including glycemia, visceral obesity, lipid profile, and creatinine, were not available. The lack of information on adverse outcomes at follow-up precludes the ability to confirm the prognostic importance of office and ambulatory PWV and AIx. In addition, office BP measurements were performed in the presence of medical personnel, an approach that has been supported by current BP guidelines [3, 4], but might have potentiated the white-coat phenomenon.

In conclusion, the present results suggest that individuals with masked BP phenotypes are more predisposed to have adverse out-of-office vascular characteristics, while individuals with white-coat BP phenotypes have adverse office and out-of-office vascular characteristics compared with individuals with normal BP levels. These data might contribute to explaining the adverse outcomes reported for individuals with white-coat and masked BP elevation [6–8].

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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