Masked Hypertension and Prehypertension: Diagnostic Overlap and Interrelationships With Left Ventricular Mass: The Masked Hypertension Study

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BACKGROUND
Masked hypertension (MHT) and prehypertension (PHT) are both associated with an increase in cardiovascular disease (CVD) risk, relative to sustained normotension. This study examined the diagnostic overlap between MHT and PHT, and their interrelationships with left ventricular (LV) mass index (LVMI), a marker of cardiovascular end-organ damage.

METHODS
A research nurse performed three manual clinic blood pressure (CBP) measurements on three occasions over a 3-week period (total of nine readings, which were averaged) in 813 participants without treated hypertension from the Masked Hypertension Study, an ongoing worksite-based, population study. Twenty-four-hour ambulatory blood pressure (ABP) was assessed by using a SpaceLabs 90207 monitor. LVMI was determined by echocardiography in 784 (96.4%) participants.

RESULTS
Of the 813 participants, 769 (94.6%) had normal CBP levels (<140/90 mm Hg). One hundred and seventeen (15.2%) participants with normal CBP had MHT (normal CBP and mean awake ABP ≥135/85 mm Hg) and 287 (37.3%) had PHT (mean CBP 120–139/80–89 mm Hg). 83.8% of MHT participants had PHT and 34.1% of PHT participants had MHT. MHT was infrequent (3.9%) when CBP was optimal (<120/80 mm Hg). After adjusting for age, gender, body mass index (BMI), race/ethnicity, history of high cholesterol, history of diabetes, current smoking, family history of hypertension, and physical activity, compared with optimal CBP with MHT participants, LVMI was significantly greater in PHT without MHT participants and in PHT with MHT participants.

CONCLUSIONS
In this community sample, there was substantial diagnostic overlap between MHT and PHT. The diagnosis of MHT using an ABP monitor may not be warranted for individuals with optimal CBP.

In 2002, Dr Thomas Pickering and our group introduced the term masked hypertension (MHT)[1] to describe individuals with normal clinic blood pressure (CBP) levels (<140/90 mm Hg) and ambulatory hypertension (awake ≥135/85 mm Hg). MHT is associated with increased left ventricular (LV) mass,[2] a marker of cardiovascular end-organ damage, and an increased risk of cardiovascular disease (CVD) events, that is significantly more than in sustained normotension (clinic and ambulatory normotension).[3–7] The confluence of increased CVD risk, a failure to be diagnosed by the conventional approach of blood pressure measurement in the clinic setting, and relatively high prevalence[8–11] makes MHT a public health concern.

Epidemiologic studies have shown that CBP in the prehypertension (PHT) range (i.e., mean systolic blood pressure (SBP) 120–139 mm Hg or mean diastolic blood pressure (DBP) 80–89 mm Hg) confer an increased CVD risk.[12] PHT is associated with higher levels of LV mass[13] and also a higher risk of CVD events,[12] compared to optimal blood pressure levels (<120/80 mm Hg).

Recent evidence suggests that CBP levels are significantly higher among individuals with MHT compared to individuals with sustained normotension,[9] despite both groups having CBP levels in the normal range (<140/90 mm Hg). These findings suggest that the prevalence of PHT may be disproportionally higher in MHT than in sustained normotension, or alternatively that the prevalence of MHT may be higher in PHT than in those with optimal CBP. These hypotheses have not been directly examined in previous studies, particularly when out-of-office blood pressure is determined by an ambulatory blood pressure (ABP) monitoring. Furthermore, the relative contributions of MHT and PHT to CVD risk are also unclear. The primary aim of this study was to evaluate the

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degree of diagnostic overlap between MHT and PHT in a large community sample, and to secondarily investigate their inter-relations with LV mass, a marker of cardiovascular end-organ damage.

METHODS

Study population. The Masked Hypertension Study, an ongoing population-based study of the prevalence, predictors, and prognosis of MHT, is comprised of employees recruited from Stony Brook University, University Hospital at Stony Brook, Columbia University Medical Center, and a private hedge fund management organization in New York. The current analysis includes 813 participants, enrolled between February 2005 and August 2010; 2,381 were screened during this period. Participants were excluded if they were <18 years of age (n = 176); taking antihypertensive or other medications that are known to affect blood pressure (n = 431); had a history of CVD or major arrhythmias including atrial fibrillation (n = 17); had evidence of secondary hypertension other than a history of pregnancy-induced hypertension, chronic renal failure (creatinine >1.6 mg/dl), liver disease, adrenal disease, or thyroid disease (n = 28); had a screening clinic SBP >160 mm Hg or DBP >105 mm Hg (n = 18); pregnant (n = 13); working <20 h a week (n = 32); non-English speaking (n = 5); had active substance abuse or a severe debilitating psychiatric disorder (n = 7); or were not interested (n = 508), not available (n = 52), or dropped out before starting the study (n = 118). For our analysis, another 163 participants were excluded due to pending study visits or had dropped out during the study, resulting in available data from 813 participants. The blood pressure eligibility criterion for this study was chosen to obtain a sample with a wide distribution of untreated blood pressures. For safety reasons, we referred participants immediately to their physicians for further management if their screening CBP was >160/105 mm Hg. Information about demographics, cardiovascular risk factors, and family history of hypertension were ascertained from participant interview. Written informed consent was obtained from all subjects. The study was approved by the Institutional Review Boards of Columbia University and Stony Brook University.

Study procedures. Participants attended five visits over a 4-week period. During the first 3 visits (visit 1–3), which occurred during a 3-week period, the participant was escorted into an examination room and asked to rest in the seated position for at least 5 min, after which a research nurse/technician obtained three CBP readings at 2-min intervals using a mercury sphygmomanometer and stethoscope.[14] Arm circumference was measured, and appropriate-sized cuffs were utilized for blood pressure assessment.[14] Thus, a total of nine CBP readings were available for each participant. On visit 3, the participant was fitted with an appropriate-sized arm cuff for a Spacelabs ABP monitor (ABPM) (Model 90207; Spacelabs, Redmond, WA). ABP measurements were taken at 28-min intervals throughout the subsequent 24-h monitoring period. The recording was analyzed to obtain average awake and sleep SBP and DBP levels,

based on sleep and awake times defined by data obtained from an actigraphy monitor worn on the wrist (ActiWatch; Phillips Respironics, Murrayville, PA), supplemented by diary reports of the times subjects woke up and went to sleep. During the awake period, participants wore a second actigraphy monitor on the waist (Actical; Phillips Respironics) to determine the level of physical activity.[15]

At visit 5, fasting blood samples were drawn from participants for determining total cholesterol, triglycerides, and high-density lipoprotein cholesterol concentrations. The Friedewald equation was used to calculate low-density lipoprotein cholesterol. M-mode, and two-dimensional echocardiograms were also performed and stored in a DICOM digital format for off-line analysis. Echocardiographers blinded to patients' clinical characteristics and blood pressure levels performed LV measurements (LVIDd, LV internal diameter during diastole; IVSd, interventricular septal thickness during diastole; and PWTd, posterior wall thickness during diastole), according to the recommendations of the American Society of Echocardiography.[16] LV mass was calculated using the corrected American Society of Echocardiography method: $0.8 \times (1.04 \times ((\text{IVSd} + \text{LVIDd} + \text{PWTd})^3 - \text{LVIDd}^3)) + 0.6$. LV mass index (LVMI) was calculated by dividing LV mass by estimated body surface area. Of the 813 participants, 784 (96.4%) underwent the echocardiography examination and had images of sufficient quality for LVMI determination. Compared to participants with available LVMI data (N = 784), participants without available LVMI data (N = 29) were younger (39.8 ± 11.6 years vs. 45.3 ± 10.3 years, P < 0.01) and had a greater body mass index (BMI) (36.6 ± 3.7 years vs. 27.5 ± 5.3 kg/m^2, P < 0.01). There were no group differences in gender (P = 0.46), race (P = 0.40), and ethnicity (P = 0.97).

Hypertension categories defined by CBP and ABP. For the primary analysis, the nine CBP readings were used to estimate mean CBP. Clinic hypertension was defined as a mean SBP ≥140 mm Hg or mean DBP ≥90 mm Hg. Ambulatory hypertension, based on mean awake ABP, was defined as mean SBP ≥135 mm Hg or mean DBP ≥85 mm Hg.[14] Participants without clinic hypertension were categorized either as having PHT, defined by mean SBP 120–139 mm Hg or mean DBP 80–89 mm Hg, or as having optimal blood pressure levels, defined by mean SBP <120 mm Hg and mean DBP <80 mm Hg.[17] MHT was defined as having clinic normotension and ambulatory hypertension. Sustained hypertension was defined as having both clinic and ambulatory hypertension. Sustained normotension was defined by having both normal CBP and ABP levels. White coat hypertension was defined as having clinic hypertension without ambulatory hypertension.

The participants in whom LVMI was assessed were divided into three groups: optimal CBP and normal awake ABP, MHT, and/or PHT, and sustained hypertension. Participants in the MHT and/or PHT group were further divided into three subgroups: optimal CBP with MHT (mean CBP levels in the optimal range with ambulatory hypertension), PHT without

MHT (i.e., mean CBP levels in the PHT range and ambulatory normotension), and PHT with MHT (mean CBP levels in the PHT range and ambulatory hypertension).

Statistical analyses. Results are expressed as numbers, percentages, mean ± s.d., and/or adjusted mean ± s.e. The number and percentage of clinic normotensive participants with PHT and MHT was determined as was the prevalence of PHT in participants with sustained normotension. To address the secondary aim of the study, one-way analysis of variance was first used to assess group differences in LVMI. Participants with white coat hypertension were excluded from these analyses. Analysis of covariance was also used to evaluate LVMI differences after adjusting for age, gender, BMI, race (African American or not), and ethnicity (Hispanic or not) (model 1). A second multivariable model (model 2) was estimated that additionally controlled for self-reported history of high cholesterol (diagnosed by a physician), self-reported history of diabetes (diagnosed by a physician), current smoking status, family history of hypertension (including 1st degree relatives and/or grandparents), and physical activity (determined by the Actical monitor). Since most studies assess CBP at only one visit, we performed sensitivity analyses in which the three CBP readings from visit 1 were used to estimate mean CBP levels. Statistical analyses were performed using SPSS v.18.0 (SPSS, Chicago, IL).

RESULTS

Table 1 shows the characteristics of the 813 study participants. Of the 44 participants with clinic hypertension based on the mean of 9 CBP readings, 36 (81.8%) had sustained hypertension and 8 (18.2%) had white coat hypertension. For both systolic and diastolic BP, CBP was significantly lower than awake ABP ($P < 0.001$).

Diagnostic overlap between MHT and PHT in participants with normal CBP levels

Based on the mean of nine CBP readings, the correlation coefficients between CBP and awake ABP were 0.75 ($P < 0.001$) and 0.64 ($P < 0.001$) for SBP and DBP, respectively. Of the 769 participants with normal CBP levels, 652 (84.8%) had sustained normotension and 117 (15.2%) had MHT; 287 (37.3%) had PHT. 98 participants had both MHT and PHT, constituting 83.8% (98/117) of those with MHT, and 34.1% (98/287) of those with PHT (**Figure 1**). The prevalence of PHT was higher among those with MHT (83.8%) than among those with sustained normotension (29.0% = 189/652). **Figure 2** shows the number and proportion with MHT by categories of normal CBP. The prevalence of MHT was higher in participants with CBP in the PHT range (34.1%) compared to those with optimal CBP (3.9%). Although the number of participants with MHT was greater in the lower half of the PHT range (53 participants in the lower half vs. 45 participants in the upper half), the proportional risk of MHT was higher in the upper half of the PHT range (51.7% in the upper half vs. 26.5% in the lower half).

Table 1 | Characteristics of the masked hypertension study participants

Characteristics	$N = 813$
Age, years	45.1 ± 10.4
Sex, % female	58.4
Race/ethnicity	
% Black or African-American	6.5
% Hispanic	10.6
Body mass index, kg/m²	27.6 ± 5.3
History of high cholesterol, %	26.1
Total cholesterol, mg/dl	194 ± 37.9
Triglycerides, mg/dl	106.1 ± 73.1
HDL, mg/dl	58.4 ± 16.8
LDL, mg/dl	114.7 ± 33.9
History of diabetes, %	3.6
Current smoking, %	7.8
Family history of hypertension, %	64.1
Physical activity,[a] mean counts/min	267.8 ± 207.9
Clinic blood pressure (mean of nine readings)	
Systolic blood pressure, mm Hg	116.2 ± 11.6
Diastolic blood pressure, mm Hg	75.4 ± 7.7
% Hypertensive[b]	5.4
% Prehypertensive[c]	35.3
% Optimal[d]	59.3
Clinic blood pressure (mean of three readings)	
Systolic blood pressure, mm Hg	116.3 ± 13.0
Diastolic blood pressure, mm Hg	76.0 ± 9.0
% Hypertensive[b]	8.9
% Prehypertensive[c]	37.0
% Optimal[d]	54.1
Ambulatory blood pressure (mean awake)	
Systolic blood pressure, mm Hg	123.1 ± 10.3
Diastolic blood pressure, mm Hg	77.4 ± 7.4
% Hypertensive[e]	18.8
Ambulatory (mean sleep)	
Systolic blood pressure, mm Hg	106.2 ± 10.6
Diastolic blood pressure, mm Hg	62.0 ± 7.8
% Hypertensive[f]	18.9

HDL, high-density lipoprotein; LDL, low-density lipoprotein.
[a]796 (97.9%) of the 813 participants had available mean physical activity data. [b]Defined by systolic blood pressure ≥140 or diastolic blood pressure ≥90 mm Hg. [c]Defined by systolic blood pressure 120–139 or diastolic blood pressure 80–89 mm Hg. [d]Defined by systolic blood pressure <120 and diastolic blood pressure <80 mm Hg. [e]Defined by systolic blood pressure ≥135 or diastolic blood pressure ≥85 mm Hg. [f]Defined by systolic blood pressure ≥120 or diastolic blood pressure ≥70 mm Hg.

Differences in LVMI across blood pressure groups

Based on the mean of 9 CBP readings, 446 participants had optimal CBP and normal awake ABP, 295 had MHT and/or PHT, and 35 had sustained hypertension. Group differences were seen in age, gender, Hispanic ethnicity, BMI, history of high cholesterol, total cholesterol, triglycerides, high-density lipoprotein, low-density lipoprotein, CBP, and awake and sleep
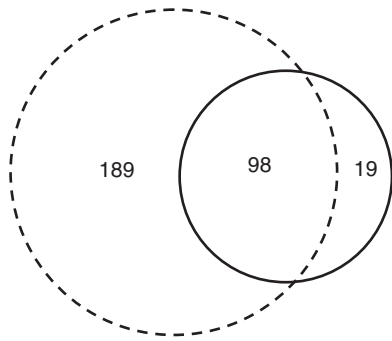
Figure 1 | Diagnostic overlap between masked hypertension and prehypertension based on the mean of nine clinic blood pressure readings. Circle with solid line represent participants with masked hypertension. Circle with dotted line represent the participants with prehypertension. Of the 769 participants with normal clinic blood pressure, a total of 117 participants had masked hypertension and 287 participants had prehypertension. 98 participants had both masked hypertension (MHT) and prehypertension (PHT), constituting 83.8% (98/117) of those with MHT, and 34.1% (98/287) of those with PHT.
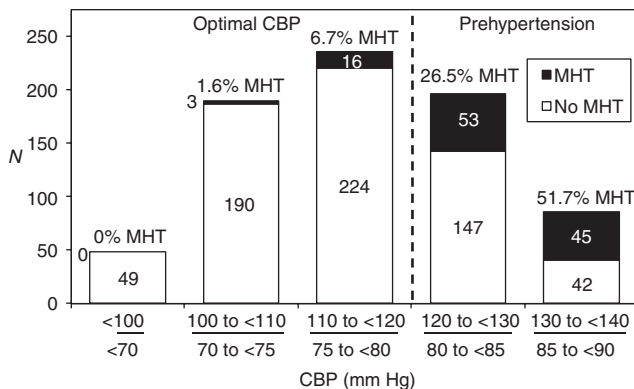
Figure 2 | Distribution of masked hypertension across clinic blood pressure categories in the normal range (<140/90 mm Hg) based on the mean of nine readings. Clinic blood pressure levels in the normal range were categorized as follows: mean SBP ≥130 mm Hg or mean DBP ≥85 mm Hg (with mean SBP <140 mm Hg and mean DBP <90 mm Hg); mean SBP ≥120 mm Hg or mean DBP ≥80 mm Hg (with mean SBP <130 mm Hg and mean DBP <85 mm Hg); mean SBP ≥110 mm Hg or mean DBP ≥75 mm Hg (with mean SBP <120 mm Hg and mean DBP <80 mm Hg); mean SBP ≥100 mm Hg or mean DBP ≥70 mm Hg (with mean SBP <110 mm Hg and mean DBP <75 mm Hg); and mean SBP <100 mm Hg and mean DBP <70 mm Hg. Of the 769 participants with normal clinic blood pressure, a total of 287 participants had prehypertension and 482 had optimal clinic blood pressure levels. The risk of masked hypertension was disproportionally concentrated among those participants with prehypertension. CBP, clinic blood pressure; DBP, diastolic blood pressure; MHT, masked hypertension; SBP, systolic blood pressure.

ABP (see **Supplementary Table S1** online). There were significant differences in LVMI across the three groups (**Table 2**, one-way analysis of variance, $P < 0.001$). Compared to participants with optimal CBP and normal awake ABP, LVMI was significantly greater in participants with MHT and/or PHT ($P < 0.001$) and in participants with sustained hypertension ($P < 0.001$). LVMI was also significantly greater in sustained hypertension participants compared to those with MHT and/or PHT ($P < 0.01$). These differences remained significant in adjusted models (models 1 and 2, **Table 2**).

Table 2 | Left ventricular mass index in participants with optimal CBP with normal awake ABP, MHT, and/or PHT, and sustained HT based on the mean of nine CBP readings

	Optimal CBP with normal awake ABP (N = 446)	MHT and/or PHT (N = 295)	Sustained HT (N = 35)	P value
				P < 0.001 (one-way ANOVA)
Unadjusted	59.0 ± 13.7	66.2 ± 15.3	73.3 ± 17.0	P1 < 0.001
				P2 < 0.001
				P3 < 0.01
				P < 0.01 (ANCOVA)
Model 1[a]	60.8 ± 0.7	64.0 ± 0.8	69.0 ± 2.3	P1 = 0.01
				P2 < 0.01
				P3 = 0.04
				P < 0.001 (ANCOVA)
Model 2[b]	60.8 ± 0.7	64.2 ± 0.8	69.2 ± 2.4	P1 < 0.01
				P2 < 0.01
				P3 = 0.045

Data are crude means ± s.d. (unadjusted model) or adjusted means ± s.e. (models 1 and 2). P1 = comparison of optimal CBP with normal awake ABP vs. MHT and/or PHT. P2 = comparison of optimal CBP with normal awake ABP vs. sustained HT. P3 = comparison of MHT and/or PHT vs. sustained HT.
ABP, ambulatory blood pressure; ANCOVA, analysis of covariance; ANOVA, analysis of variance; CBP, clinic blood pressure; HT, hypertension; MHT, masked hypertension; PHT, prehypertension.
[a]Model 1 adjusts for age, sex, body mass index, race, and ethnicity. [b]Model 2 adjusts for covariates in model 1 + history of high cholesterol, history of diabetes, current smoking status, family history of hypertension, and physical activity.

Of the 295 participants in the MHT and/or PHT group, 18 participants had optimal CBP with MHT, 180 had PHT without MHT, and 97 had PHT with MHT. Differences in gender, BMI, CBP, and awake and sleep ABP were seen across these subgroups (**Table 3**). There were significant group differences in LVMI (**Table 4**, one-way analysis of variance, $P < 0.001$). Compared with optimal CBP with MHT participants, LVMI was significantly greater in PHT without MHT participants ($P < 0.01$) and in PHT with MHT participants ($P < 0.001$). LVMI was also significantly greater in PHT with MHT participants compared to PHT without MHT participants ($P = 0.04$). After adjustment for age, gender, BMI, race and ethnicity (model 1, **Table 4**), there was no longer a significant difference in LVMI between participants with PHT without MHT and PHT with MHT ($P = 0.19$). All other group differences remained significant. Results were similar after adjustment for additional covariates (model 2, **Table 4**).

Sensitivity analyses

The pattern of results was similar when mean CBP was estimated from three readings. Of the 72 participants with clinic hypertension based on the mean of three CBP readings, 50 (69.4%) had sustained hypertension and 22 (30.6%) had white coat hypertension. For both systolic and diastolic

Table 3 | Characteristics of participants who underwent echocardiographic assessment of left ventricular mass index and were classified as having optimal CBP with MHT, PHT without MHT, and PHT with MHT based on the mean of nine CBP readings

Characteristics	Optimal CBP with MHT (N = 18)	PHT without MHT (N = 180)	PHT with MHT (N = 97)	P value[a]
Age, years	44.7 ± 9.4	47.8 ± 10.4	48.4 ± 9.5	0.34
Sex, % female	72.2	52.2	34.0	<0.01
Race/ethnicity				
% Black	5.6	6.7	9.3	0.7
% Hispanic	0.0	7.2	8.2	0.46
Body mass index, kg/m^2	26.6 ± 5.8	30.1 ± 5.6	28.8 ± 4.8	0.01
History of high cholesterol, %	16.7	31.1	26.8	0.38
Total cholesterol, mg/dl	188.3 ± 39.3	198.8 ± 40.9	201.4 ± 41.9	0.47
Triglycerides, mg/dl	98.8 ± 53.5	121.6 ± 68.3	138.7 ± 118.3	0.12
HDL, mg/dl	62.3 ± 14.7	54.8 ± 17.4	52.9 ± 14.6	0.09
LDL, mg/dl	106.3 ± 36.7	119.6 ± 36.3	122.3 ± 37.9	0.24
History of diabetes, %	0.0	6.1	1.0	0.08
Current smoking, %	16.7	8.9	5.2	0.22
Family history of hypertension, %	72.2	70	63.9	0.54
Physical activity,[b] mean counts/min	374.1 ± 314.9	266.9 ± 239.5	254.9 ± 167.1	0.17
Clinic (mean)				
Systolic blood pressure, mm Hg	112.8 ± 4.5	124.4 ± 5.4	126.7 ± 6.2	<0.001
Diastolic blood pressure, mm Hg	74.9 ± 3.0	80.0 ± 4.4	82.3 ± 4.4	<0.001
Ambulatory (mean awake)				
Systolic blood pressure, mm Hg	131.6 ± 5.9	125.4 ± 5.9	135.7 ± 7.2	<0.001
Diastolic blood pressure, mm Hg	86.6 ± 4.1	77.5 ± 5.4	86.9 ± 4.6	<0.001
Ambulatory (mean sleep)				
Systolic blood pressure, mm Hg	110.0 ± 6.1	108.6 ± 8.5	116.5 ± 9.8	<0.001
Diastolic blood pressure, mm Hg	66.2 ± 4.8	63.0 ± 6.2	69.7 ± 6.5	<0.001

ANOVA, analysis of variance; CBP, clinic blood pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein; MHT, masked hypertension; PHT, prehypertension.
[a]One-way ANOVA for continuous variables. χ2 for categorical variables. [b]Of the 784 participants who underwent echocardiography and had assessment of left ventricular mass index, 767 (97.8%) had available mean physical activity. 0 (0%) of the 18 optimal CBP with MHT participants, 4 (2.2%) of the 180 PHT without MHT participants, and 5 (5.2%) of the 97 PHT with MHT participants did not have mean physical activity data.

BP, CBP was significantly lower than awake ABP (P < 0.001). Of the 741 participants with normal CBP levels, 638 (86.1%) had sustained normotension and 103 (13.9%) had MHT; 301 (40.6%) had PHT. **Supplementary Figure S1** online shows substantial diagnostic overlap between MHT and PHT. Furthermore, the prevalence of PHT was higher among those with MHT (75.7%) than among those with sustained normotension (35.0% = 223/638). **Supplementary Figure S2** online shows the number and proportion of MHT by categories of normal CBP. The prevalence of MHT was higher in participants with CBP in the PHT range (25.9%) compared to those with optimal CBP (5.7%).

Characteristics of participants with available LVMI by group (optimal CBP and normal awake ABP, MHT and/or PHT, and sustained hypertension) and subgroup (optimal CBP with MHT, PHT without MHT, and PHT with MHT) are presented in **Supplementary Tables S2** and **S3** online. Mean LVMI by group and subgroup are shown in **Supplementary Tables S4** and **S5** online.

Finally, as nocturnal hypertension is associated with increased CVD risk,[18] additional analyses were performed in which nocturnal hypertension (mean sleep ABP ≥120/70 mm Hg) was added to model 2 for the analyses in which mean CBP was estimated from nine readings. The relations across groups remained unchanged (data not shown). Nocturnal hypertension also had no impact on the individual relations of PHT and MHT with LVMI (interaction P = 0.99 between nocturnal hypertension and PHT, interaction P = 0.13 between nocturnal hypertension and MHT).

DISCUSSION

This study adds important information to the literature on MHT diagnosis. In our study, there were several principal findings. There was substantial diagnostic overlap between MHT and PHT in clinic normotensive participants. The prevalence of MHT was relatively high in participants with PHT and low in participants with optimal CBP. Furthermore, the prevalence of PHT was greater in MHT than in sustained normotension.

Table 4 | Left ventricular mass index in participants with optimal CBP with MHT, PHT without MHT, and PHT with MHT based on the mean of nine CBP readings

	Optimal CBP with MHT (N = 18)	PHT without MHT (N = 180)	PHT with MHT (N = 97)	P value
Unadjusted	52.8 ± 10.9	65.7 ± 14.1	69.5 ± 16.7	P < 0.001 (one-way ANOVA)
				P1 < 0.01
				P2 < 0.001
				P3 = 0.04
Model 1[a]	56.9 ± 3.4	66.0 ± 1.1	68.4 ± 1.4	P < 0.01 (ANCOVA)
				P1 = 0.01
				P2 < 0.01
				P3 = 0.19
				P = 0.01 (ANCOVA)
Model 2[b]	57.3 ± 3.4	66.1 ± 1.1	68.6 ± 1.5	P1 = 0.01
				P2 < 0.01
				P3 = 0.19

Data are crude means ± s.d. (unadjusted model) or adjusted means ± s.e. (models 1 and 2). P1 = comparison of Optimal CBP with MHT vs. PHT without MHT. P2 = comparison of Optimal CBP with MHT vs. PHT with MHT. P3 = comparison of PHT without MHT vs. PHT with MHT.

ANCOVA, analysis of covariance; ANOVA, analysis of variance; CBP, clinic blood pressure; MHT, masked hypertension; PHT, prehypertension.

[a]Model 1 adjusts for age, sex, body mass index, race, and ethnicity. [b]Model 2 adjusts for covariates in model 1 + history of high cholesterol, history of diabetes, current smoking status, family history of hypertension, and physical activity.

In the general population, especially in younger individuals with clinic normotension, awake ABP tends to be higher than CBP.[19–22] We have hypothesized that as both CBP and ABP rise with aging, ABP first exceeds the threshold for a diagnosis of ambulatory hypertension while CBP increases but remains in the clinic normotensive range.[20,23] As demonstrated by our study, a large proportion of these individuals have PHT. We posit that the CBP of these MHT individuals eventually crosses the threshold for clinic hypertension, leading to sustained hypertension. This is supported by increasing evidence that MHT is a precursor for sustained hypertension.[24–26]

Of the MHT participants in our study, those with PHT (i.e., PHT with MHT) had significantly higher levels of LVMI than those with optimal CBP (i.e., optimal CBP with MHT). Given that ABP has superior predictive value for CVD risk over CBP, one would also anticipate that PHT with MHT would be a higher CVD risk category than PHT without MHT. However, although there was a significant unadjusted difference in LVMI between PHT with MHT and PHT without MHT participants in our study, this difference was no longer significant in adjusted models. One possible explanation for this finding is the large number and high quality of CBP readings (average of nine readings taken on three separate occasions according to published guidelines[14]) that were obtained and used to define mean CBP. The correlations between CBP and ABP in our study are greater than what has been observed in some previous studies,[27,28] which may have limited the ability to detect differences in LVMI between PHT participants with and without MHT. Presently, scarce data exist from prior studies as to whether MHT adds prognostic information in individuals with PHT. In what to our knowledge is the only published study to examine the predictive value of MHT for CVD events in participants with PHT, Pierdomenico et al.[29] found that in participants with PHT, MHT was associated with a significantly higher rate of CVD events, compared to those participants without MHT ("true PHT"). This study was limited by a small number of events (18 events in MHT and PHT vs. 11 events in true PHT) and potentially incomplete examination of confounders such as male gender.[29]

Also, unexpectedly in our study, compared to participants with optimal CBP with MHT, LVMI was significantly greater in participants with PHT without MHT in adjusted models. In addition to the number and quality of CBP readings, which likely increased the predictive value of CBP, there are other plausible explanations for these findings. First, notably, as it is relatively rare for an individual with optimal CBP to have MHT, the sample size of the optimal CBP with MHT group was small. Additionally, variability in ABPM[30] may have also allowed for some participants with optimal CBP and normal awake ABP to be incorrectly categorized as having optimal CBP and ambulatory hypertension, leading to a lower than expected LVMI in the optimal CBP with MHT group.

These issues have important clinical implications. If MHT is a high-risk subgroup of the larger PHT group, then it may be appropriate to recommend that individuals with PHT receive targeted screening for MHT using ABPM. Furthermore, if optimal CBP with MHT is a lower CVD risk group, then ABPM may not be indicated for individuals with optimal CBP levels, particularly as the prevalence of MHT is low in this group.

Whether our results on the diagnostic overlap between MHT and PHT can be extended to home blood pressure monitoring is unknown. Findings from the Self measurement of blood pressure at Home in the Elderly: Assessment and Follow-up (SHEAF) study[31], the Japan Home vs. Office BP Measurement Evaluation (J-HOME) study[32], and a substudy of the Three-City Study (3C)[33] indicate that clinic SBP in the PHT range is associated with MHT, when determined by home blood pressure monitoring. These findings may not be directly comparable to the results of our study. In addition to the reliance on home blood pressure monitoring, these studies included treated hypertensive patients. Further, participants were older, and many had prevalent CVD.

There are several possible limitations to our study. First, as awake ABP was estimated from one 24-h monitoring period, we cannot exclude the possibility that the study results would have differed with the inclusion of additional 24-h period. Multiple, high quality readings were used in our study to estimate CBP. Nonetheless, this approach is consistent with published guidelines, which recommend the performance

of measurements in this manner to estimate CBP.[14] Finally, our sample consisted of adult employees who were generally healthy. Whether our results can be extended to other populations remains unknown.

Major strengths of the study include a large sample size, the inclusion of a large proportion of participants with normal CBP levels, the exclusion of participants on antihypertensive medications, and consideration of several possible confounding factors including physical activity. Further, echocardiography with the assessment of LVMI was successfully performed in almost all participants. Finally, as this is one of the first studies to directly examine the degree of diagnostic overlap between MHT and PHT in a community sample, and to investigate their respective relationships with a marker of cardiovascular end-organ damage, the current study provides valuable new information.

In conclusion, the results of the present study demonstrate that in an employed, community sample, there is substantial diagnostic overlap between MHT and PHT in individuals with clinic normotension. Furthermore, given the low prevalence of MHT in individuals with optimal CBP, our findings suggest that the diagnosis of MHT using an ABPM may not be warranted for individuals with optimal CBP. Future studies should confirm our findings, and additionally examine the relative contributions of PHT and MHT to CVD event risk.

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