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Masked hypertension in a middle-aged population and its relation to manifestations of vascular disease

Peder af Geijerstam[a], Jan Engvall[a,b,c], Carl Johan Östgren[a,b], Karin Rådholm[a,d], and Fredrik H. Nyström[a]

Background: Masked hypertension is associated with cardiovascular disease (CVD). However, previous large studies have not used the same device to measure office and home blood pressure (BP) and adhered to current home BP measurement recommendations of the European Society of Hypertension. We aimed to characterize masked hypertension and explore its relation to manifestations of CVD.

Methods: A randomly selected cohort of 5057 participants aged 50–64 years from the Swedish CardioPulmonary BioImage Study (SCAPIS) was evaluated with office and home BP using the semi-automatic Omron M10-IT oscillometric device. Additional analyses included pulse wave velocity (PWV) and coronary artery calcium score (CACS).

Results: Of participants, 4122 did not have current antihypertensive treatment, and were thus included in our analyses. Of these, 2634 (63.9%) had sustained normotension, and 172 (4.2%) had masked hypertension. Participants with masked hypertension vs. sustained normotension were more often men (66.9 vs. 46.2%, $P < 0.001$). Those with masked hypertension had higher mean PWV [9.3 (95% confidence interval, 95% CI 9.1–9.5) vs. 8.3 (95% CI 8.2–8.4) m/s, $P < 0.001$] and odds ratio for CACS at least 100 [1.65 (95% CI 1.02–2.68), $P = 0.040$]. These associations were similar in a posthoc analysis of masked hypertension and sustained normotension, matched for age, sex and systolic office BP.

Conclusion: Masked hypertension was associated with markers of CVD. This suggests that home BP is a better predictor of risk, even when the recordings are performed with the same measurement device, in a population-based setting with randomized recruitment.

Graphical abstract: http://links.lww.com/HJH/C174

Keywords: blood pressure, cardiovascular disease, carotid artery plaques, coronary artery calcium score, home blood pressure, masked hypertension, pulse wave velocity

Abbreviations: BP, blood pressure; CACS, coronary artery calcium score; CKD-EPI, the Chronic Kidney Disease Epidemiology Collaboration equation; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; ESH, European Society of Hypertension; HbA1c, glycated haemoglobin; HBPM, home blood pressure monitoring; HDL, high-density lipoprotein; hsCRP, high sensitivity C-reactive protein; LDL, low-density lipoprotein; PWV, pulse wave velocity; SCAPIS, The Swedish CardioPulmonary BioImage Study; WCH, white-coat hypertension

INTRODUCTION

Elevated blood pressure (BP), both at the office and out-of-office, independently and continuously increases the risk of cardiovascular disease (CVD) [1]. To diagnose and monitor hypertension, out-of-office BP measurements have several benefits over office BP measurements, including better predicting cardiovascular mortality [2]. Combining office BP with home BP monitoring (HBPM) makes it possible to diagnose intermediate hypertension phenotypes [3].

Masked hypertension is defined as elevated HBPM despite normal office BP [3]. In the general population, the prevalence of masked hypertension is between 9 and 25% [4,5]. Masked hypertension is associated with an increased risk of cardiovascular events [6–8]. Previous studies have also found associations with higher BMI, higher total cholesterol, smoking, diabetes mellitus and history of CVD, as well as end-organ damage including chronic kidney disease, left ventricular hypertrophy and carotid intima-media thickness, and increased pulse wave velocity (PWV) [5,7–13].

Three previous cohort studies of HBPM have investigated large (at least 1000 participants), randomly selected populations [8,14–16]. However, no previous studies have used the same BP device at the office and at home, and followed the current recommendations to record the HBPM both in the morning and evening for at least 3 days [2]. Thus, the aim of our study was to cross-sectionally characterize

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[a]Department of Health, Medicine and Caring Sciences, Faculty of Medicine and Health Sciences, [b]Center of Medical Image Science and Visualization, [c]Department of Clinical Physiology, Linköping University, Linköping, Sweden and [d]The George Institute for Global Health, University of New South Wales, Sydney, New South Wales, Australia

Correspondence to Peder af Geijerstam, Linköping University, SE-581 83 Linköping, Sweden. Tel: +46 073 9597426; e-mail: peder.af.geijerstam@liu.se

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masked hypertension in a large, randomly selected population and explore its relation to manifestations of vascular disease, including the extent of coronary artery calcium score (CACS) on diagnostic imaging and the presence of carotid artery plaques on ultrasound.

MATERIALS AND METHODS

Study population

The Swedish CardioPulmonary BioImage Study (SCAPIS) is a prospective observational study including 30 000 men and women aged 50–64 years, randomly selected from the Swedish population register [17]. The overall participation rate was 50.3%, evenly distributed between men and women, and in the Linköping cohort 58%, supplementary Figure 1, http://links.lww.com/HJH/C170 [18]. In brief, the study data include anthropometric measurements, clinical physiology and imaging studies, blood analyses, as well as 175 questionnaire questions of various topics including lifestyle [17]. A subsample in Linköping of 5057 participants was also evaluated with HBPM, in addition to the regular office BP measurements.

Measurement of blood pressure and definition of blood pressure classification

Office and home BP were measured according to a previously published protocol [19]. In brief, all measurements were taken using the semi-automatic Omron M10-IT oscillometric device (Omron, Kyoto, Kyoto prefecture, Japan) after 5 min rest. Instructions included no smoking, coffee intake or strenuous activity 1 h before measurements. Office BP was reported as the highest mean of two consecutive measurements from each arm in the supine position. For HBPM, SBP and DBP were measured in the sitting position three times in the morning and three times in the evening for 7 days except from the first day, where only evening measurements were taken.

When classifying office BP, observations with a SBP of 140 mmHg or higher and/or a DBP of 90 mmHg or higher were defined as elevated, and those with both measurements below these levels were defined as normotensive. When classifying HBPM, observations with a SBP of 135 mmHg or higher and/or a DBP of 85 mmHg or higher were defined as elevated, and those with both measurements below these levels were defined as normotensive. BP was then classified as either 'sustained normotension' if both office and home BP were normotensive, 'sustained hypertension' if both office and home BP were elevated, 'masked hypertension' if office BP was normotensive, but HBPM was elevated, or 'white-coat hypertension' if office BP was elevated, but HBPM was normotensive.

The difference between office BP and HBPM ('office-home BP difference') was calculated for each individual by subtracting the HBPM from the office BP.

Additional measurements and imaging

PWV was measured according to a previously published protocol [20] using the SphygmoCor XCEL system (from AtCor Medical, Sydney, New South Wales, Australia), and calculated using a correction factor of 0.8 in accordance with current international guidelines [21].

The presence of carotid artery plaques was investigated bilaterally using a Siemens Acuson S2000 ultrasound scanner equipped with a 9L4 linear transducer (both from Siemens Healthineers, Erlangen, Germany) [22].

The presence of coronary artery calcifications was assessed using a SOMATOM Definition Flash computer tomography scanner (from Siemens Medical Solution, Forchheim, Germany), and quantified as CACS using the Agatston score, as previously described [23].

Statistical analyses

Distributions were determined using a Kolmogorov–Smirnov test as well as visual assessment. Continuous variables were shown as the mean and standard deviation, and differences between BP classifications were tested using a two-sided Mann–Whitney *U* test. Categorical variables were shown as the frequency and percentage, and differences between BP classifications were tested using the chi-squared test.

Baseline characteristics according to BP classifications were evaluated for all participants. Low-density lipoprotein (LDL) was calculated using Friedewald's formula [LDL = total cholesterol – high-density lipoprotein (HDL) – 0.45 x triglycerides]. Estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation [24], but without including race, as that was not recorded in the study.

Manifestations of vascular disease were presented in relation to BP classification: PWV was presented as the means and 95% confidence interval (95% CI); CACS (<100, and ≥ 100, and in a sensitivity analysis, <400 vs. ≥ 400) and the presence of carotid artery plaques (no plaque or one or more plaques) were presented with odds ratios (ORs) and 95% CI. A linear regression (PWV) and a generalized linear model (categorical variables) were used to analyse differences in relation to BP classifications: crude (model 1); adjusted for age and sex (model 2); and adjusted for age, sex, fasting glucose, BMI and systolic office BP (model 3). When analysing differences between masked and white-coat hypertension, however, systolic office BP was not included in model 3, as office BP is a part of the classifications.

An ad hoc matching analysis was made for participants with masked hypertension and sustained normotension on a 1–3 ratio using propensity score matching for age, sex and systolic office BP. Matching was made with a calliper of 1 standard deviation for systolic office BP and 2 standard deviations for age. Baseline characteristics were evaluated for all the matched participants, presented for sustained normotension and masked hypertension respectively. Manifestations of vascular disease in relation to BP classification were presented in the same way as described above.

Statistical tests were two-tailed and *P* values of less than 0.05 were considered statistically significant. R version 4.2.1 and RStudio version 2022.07.1 (R Foundation for Statistical Computing, Vienna, Austria) were used for data analyses.

Ethical considerations

The SCAPIS study was approved by the Regional Ethical Review board in Umeå (Dnr 2010–228–31 M) and the Regional Ethical Review board in Linköping (Dnr 2018/478–31) and adheres to the Declaration of Helsinki. For all participants, written informed consent was obtained.

RESULTS

Of 5057 included participants, 5029 participated in the HBPM monitoring. Of these, 4122 did not have antihypertensive treatment and were thus included in our analysis.

The mean age was 57.1 (SD 4.4) years, and 2020 (49.0%) of the participants were men. Of all participants, 2634 (63.9%) had sustained normotension, 172 (4.2%) had masked hypertension, 633 (15.4%) had sustained hypertension and 683 (16.6%) had white-coat hypertension. Participants with masked hypertension were compared with those with sustained normotension, more often men (66.9 vs. 46.2%, respectively, $P < 0.001$) and had a higher mean BMI [28.0 (SD 3.9) vs 25.6 (SD 3.7) kg/m^2, $P < 0.001$], Table 1. The difference in mean BMI remained when analysing men [28.2 (SD 3.3) vs. 26.1 (SD 3.3) kg/m^2, $P < 0.001$] and women [27.5 (SD 4.8) vs. 25.2 (SD 4.1) kg/m^2, $P < 0.001$] separately, Supplementary tables 1–2, http://links.lww.com/HJH/C171. Furthermore, participants with masked hypertension, compared with those with sustained normotension had a higher mean fasting glucose [5.8 (SD 1.0) vs. 5.5 (SD 0.9) mmol/l, respectively, $P < 0.001$], a lower mean HDL [1.5 (SD 0.5) vs. 1.7 (SD 0.5) mmol/l, respectively, $P < 0.001$] and a higher mean high-sensitivity C-reactive protein (hsCRP) [2.7 (SD 6.2) vs. 1.6 (SD 3.2) mg/l, respectively, $P < 0.001$], Table 1. The mean systolic office-home BP difference was lower for those with masked hypertension compared with those with sustained normotension [-2.3 (SD 7.1) vs. 8.6 (SD 8.6) mmHg, $P < 0.001$], Table 1. Compared with participants with white-coat hypertension, those with masked hypertension were more often men (66.9 vs. 44.4%, $P < 0.001$), had a higher BMI [mean (SD) 28.0 (3.9) vs. 26.9 (4.0) kg/m^2, $P < 0.001$ and higher hsCRP [mean (SD) 2.7 (6.2) vs. 1.7 (2.1) mg/l, $P = 0.021$].

The mean PWV was higher in masked hypertension compared with sustained normotension in all models [9.3 (95% CI 9.1–9.5) vs. 8.3 (95% CI 8.2–8.4) m/s, $P < 0.001$], Table 2 and Fig. 1. The OR for CACS at or above 100 was higher in those with masked hypertension in all models [1.65 (95% CI 1.02–2.68), $P = 0.040$], Table 2 and Fig. 2. In a sensitivity analysis, the OR for CACS at or above 400 was also higher in those with masked hypertension [$n = 11$ (6.4%)] compared with sustained normotension [$n = 103$ (3.9%)], OR 2.73 (1.27–5.89), $P = 0.010$, but not when adjusting for age and sex, supplementary table 5, http://links.lww.com/HJH/C171. The OR for at least one carotid artery plaque was higher in those with masked hypertension in the unadjusted model [1.48 (95% CI 1.08–2.02), $P = 0.014$], but not when adjusted for age and sex (Table 2). When comparing participants with masked hypertension to those with white-coat hypertension, no difference in PWV, CACS at least 100 or carotid artery plaques was found (Table 3). When comparing participants with masked hypertension to those with sustained hypertension, no difference in CACS at least 100 or carotid artery plaques was found, but the PWV was higher for those with sustained hypertension in all models [mean (95% CI) 10.0 (9.7–10.2) vs. 9.3 (9.1–9.6) m/s, $P < 0.001$], Table 4.

An additional post hoc matching characterization comparing participants with masked hypertension ($n = 172$) to sustained normotension ($n = 516$), matched for age, sex and systolic office BP is shown in Supplementary tables 3 and 4, http://links.lww.com/HJH/C171. Results were similar to the regression analyses of all participants, with higher systolic home BP for those with masked hypertension compared with sustained normotension, mean (SD) 132.2 (6.7) vs. 118.0 (8.0) mmHg, $P < 0.001$, Supplementary table 3, http://links.lww.com/HJH/C171. For participants with masked hypertension compared with those with sustained normotension, PWV was higher, mean (95% CI) 9.4 (9.2–9.6) vs. 8.7 (8.6–8.8) m/s, $P < 0.001$, and the OR of CACS at least 100 was similar to our initial analysis, 1.77 (95% CI 1.07–2.94), $P = 0.027$, Supplementary table 4, http://links.lww.com/HJH/C171.

DISCUSSION

This study of a large, randomly selected cohort of men and women aged 50–64 years showed an association between masked hypertension and several risk factors for CVD, as well as manifestations of vascular disease, compared with sustained normotension. Previous studies have found an association between masked hypertension and risk factors for CVD such as dysglycaemia and higher total cholesterol [8–10,25]. Our results showed associations with additional markers of increased cardiovascular risk: higher fasting glucose, lower HDL and higher hsCRP.

Our study also showed an association between masked hypertension and several manifestations of vascular disease: higher PWV, higher CACS and the presence of carotid artery plaques. The association with higher PWV and CACS at or above 100 remained in the multivariate model, as well as in a post hoc matching analysis controlling for age, sex and systolic office BP. Interestingly, PWV was even higher in those with sustained vs. masked hypertension, indicating an added risk for those with increased home BP if also office BP is increased, even though masked hypertension in and by itself was also associated with increased PWV compared with sustained normotension. However, CACS at or above 100 was the same between those with masked and sustained hypertension. PWV is a noninvasive surrogate marker of arterial stiffness, which has previously been associated with masked hypertension and cardiovascular events [9,11,26]. The association between masked hypertension and increased CACS has previously been suggested as a trend, but not confirmed as significant [27]. As for the carotid arteries, previous studies have shown an association with increased carotid intima thickness [11], but to the best of our knowledge, no previously published study has shown an association with the presence of carotid artery plaques.

Participants with masked hypertension vs. sustained normotension had elevated systolic home BP in the post hoc analysis that included matching for systolic office BP. However, the mean systolic office to home BP difference was less than 3 mmHg, indicating that small differences in SBP can make a great difference in CVD risk, in our study shown as the association with markers of CVD.

The prevalence of masked hypertension in our study was relatively low at 4.9% compared with previous findings of 9–25% [4,5]. This could result from the exclusion of

TABLE 1. Baseline characteristics according to blood pressure classification

		All participants ($N = 4122$)	Sustained normotension ($n = 2634$)	Sustained hypertension ($n = 633$)	White-coat hypertension ($n = 683$)	Masked hypertension ($n = 172$)	*P* (for MH in relation to SN, SH and WCH, respectively)
Sex, men, *n* (%)		2020 (49.0)	1216 (46.2)	386 (61.0)	303 (44.4)	115 (66.9)	<0.001 (SN, WCH), 0.158 (SH)
Age (years), mean (SD)		57.1 (4.4)	56.6 (4.3)	58.0 (4.4)	58.1 (4.5)	57.1 (4.1)	0.117 (SN), 0.018 (SH), 0.007 (WCH)
Ever-smokers, *n* (%)		1613 (39.1)	989 (37.5)	271 (42.8)	281 (41.1)	72 (41.9)	0.154 (SN), 0.905 (SH), 0.782 (WCH)
BMI (kg/m^2), mean (SD)		26.4 (4.1)	25.6 (3.7)	28.7 (4.6)	26.9 (4.0)	28.0 (3.9)	<0.001 (SN, WCH), 0.108 (SH)
Waist circumference (cm), mean (SD)		91.3 (12.3)	88.8 (11.4)	98.8 (12.6)	92.5 (11.5)	98.0 (11.5)	<0.001 (SN, WCH), 0.446 (SH)
Fasting glucose (mmol/l), mean (SD)		5.7 (1.1)	5.5 (0.9)	6.0 (1.4)	5.8 (1.2)	5.8 (1.0)	<0.001 (SN), 0.064 (SH), 0.392 (WCH)
HbA1c (mmol/mol), mean (SD)		35.6 (5.8)	35.3 (5.0)	36.6 (7.6)	36.0 (6.7)	36.0 (6.1)	0.128 (SN), 0.850 (SH), 0.879 (WCH)
eGFR (ml/min per 1.73 m^2), mean (SD)		82.6 (11.7)	82.6 (11.7)	83.4 (11.9)	82.1 (11.5)	81.6 (12.1)	0.214 (SN), 0.072 (SH), 0.558 (WCH)
Total cholesterol (mmol/l), mean (SD)		5.6 (1.0)	5.5 (1.0)	5.7 (1.1)	5.8 (1.1)	5.5 (1.0)	0.716 (SN), 0.016 (SH), 0.002 (WCH)
LDL (mmol/l), mean (SD)		3.4 (0.9)	3.3 (0.9)	3.5 (1.0)	3.5 (1.0)	3.4 (0.9)	0.242 (SN), 0.139 (SH), 0.129 (WCH)
HDL (mmol/l), mean (SD)		1.7 (0.5)	1.7 (0.5)	1.5 (0.4)	1.7 (0.5)	1.5 (0.5)	<0.001 (SN, WCH), 0.105 (SH)
Triglycerides (mmol/l), mean (SD)		1.2 (0.7)	1.1 (0.6)	1.5 (1.0)	1.3 (0.7)	1.3 (0.8)	<0.001 (SN), 0.014 (SH), 0.315 (WCH)
hsCRP (mg/l), mean (SD)		1.8 (3.5)	1.6 (3.2)	2.5 (4.7)	1.7 (2.1)	2.7 (6.2)	<0.001 (SN), 0.454 (SH), 0.021 (WCH)
Pulse wave velocity (m/s), mean (SD)		8.6 (7.8–9.5)	8.2 (7.6–8.9)	9.9 (9.0–10.9)	9.1 (8.3–10.0)	9.2 (8.6–10.0)	<0.001 (SN, SH), 0.127 (WCH)
Coronary artery calcium score ≥100, *n* (%)		376 (9.1)	184 (7.0)	82 (13.0)	83 (12.2)	27 (15.7)	<0.001 (SN), 0.358 (SH), 0.236 (WCH)
Carotid artery plaques ≥1, *n* (%)		2171 (52.7)	1260 (47.8)	403 (63.7)	409 (59.9)	99 (57.6)	0.013 (SN), 0.143 (SH), 0.579 (WCH)
Current medication, *n* (%)	Hyperlipidaemia	121 (2.9)	71 (2.7)	24 (3.8)	21 (3.1)	5 (2.9)	0.869 (SN), 0.581 (SH), 0.909 (WCH)
	Diabetes mellitus	74 (1.8)	40 (1.5)	15 (2.4)	14 (2.0)	5 (2.9)	0.160 (SN), 0.688 (SH), 0.495 (WCH)
Office BP (mmHg), mean (SD)	Systolic	130.6 (17.2)	120.9 (9.7)	154.7 (14.5)	146.1 (9.2)	129.9 (6.4)	<0.001 (SN, SH, WCH)
	Diastolic	82.3 (10.2)	76.9 (6.4)	96.5 (8.4)	90.3 (5.9)	82.8 (4.6)	<0.001 (SN, SH, WCH)
Home BP (mmHg), mean (SD)	Systolic	119.0 (13.6)	112.3 (9.3)	139.4 (10.4)	122.4 (7.5)	132.2 (6.7)	<0.001 (SN, SH, WCH)
	Diastolic	77.0 (8.6)	72.8 (6.0)	90.0 (6.1)	78.3 (4.7)	86.6 (3.8)	<0.001 (SN, SH, WCH)
Office-home BP difference (mmHg), mean (SD)	Systolic	11.7 (11.2)	8.6 (8.6)	15.2 (11.8)	23.7 (9.8)	−2.3 (7.1)	<0.001 (SN, SH, WCH)
	Diastolic	5.4 (6.9)	4.0 (5.7)	6.4 (7.3)	11.9 (6.0)	−3.8 (4.8)	<0.001 (SN, SH, WCH)
Office-home BP difference (mmHg), median (Q1-Q3)	Systolic	10.5 (3.9 to 18.2)	8.2 (2.8 to 14.0)	14.2 (7.1 to 21.9)	22.8 (16.4 to 30.4)	−1.6 (−6.3 to 2.5)	<0.001 (SN, SH, WCH)
	Diastolic	5.2 (0.6 to 9.7)	4.1 (0.1 to 7.7)	5.8 (1.6 to 11.2)	11.8 (7.9 to 15.9)	−3.3 (−7.2 to −0.5)	<0.001 (SN, SH, WCH)

Values for sex, age, BMI, waist circumference, fasting glucose, HbA1c, eGFR, total cholesterol, LDL, HDL, triglycerides, hsCRP, carotid artery plaques and office and home BP measurements were calculated based on 4084–4122 (99.1–100%) of all participants. Values for coronary artery calcium score was calculated based on 4029 (97.7%) of all participants. Values for ever-smokers were calculated based on 4013 (97.4%) of all participants. Values for pulse wave velocity was calculated based on 2854 (69.2%) of all participants. Home blood pressure measurements were based on at least three morning and three evening registrations for 4120 (99.95%) of all participants. BMI was calculated as weight (kg) divided by the square of height (m). eGFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation [24], but without including race since that variable was not recorded. LDL was calculated using Friedewald's formula (LDL = total cholesterol – HDL – 0.45 x triglycerides). The office-home BP difference was calculated for each individual by subtracting the HBPM from the office BP. Differences between BP classifications were tested using a two-sided Mann–Whitney *U* test for continuous variables and a chi-squared test for categorical variables.

BP, blood pressure; eGFR, estimated glomerular filtration rate; HbA1c, glycated haemoglobin; HDL, high-density lipoproteins; hsCRP, high-sensitivity C-reactive protein; LDL, low-density lipoproteins; MH, masked hypertension; SH, sustained hypertension; SN, sustained normotension; WCH, white-coat hypertension.

TABLE 2. Markers of cardiovascular disease in participants with masked hypertension compared to sustained normotension

	Model 1 (crude)		Model 2 (adjusted for age and sex)		Model 3 (adjusted for age, sex, fasting glucose, BMI and systolic office BP)	
	Mean (95% CI)	*P*	Mean (95% CI)	*P*	Mean (95% CI)	*P*
Pulse wave velocity (m/s)[a]						
Sustained normotension	8.3 (8.2–8.3)	–	8.3 (8.2–8.4)	–	8.3 (8.2–8.4)	–
Masked hypertension	9.4 (9.2–9.6)	<0.001	9.4 (9.1–9.7)	<0.001	9.3 (9.1–9.5)	<0.001
	OR (95% CI)	***P***	**OR (95% CI)**	***P***	**OR (95% CI)**	***P***
CACS ≥100[b]	2.47 (1.60–3.83)	<0.001	1.88 (1.19–2.97)	0.007	1.65 (1.02–2.68)	0.040
Carotid artery plaques ≥1[c]	1.48 (1.08–2.02)	0.014	1.33 (0.97–1.83)	0.077	1.12 (0.80–1.56)	0.521

Pulse wave velocity (PWV) was calculated using a correction factor of 0.8 in accordance with current international guidelines [21]. Differences between means were tested using linear regression, and differences between odds ratios were tested using a generalized linear model. When comparing values for participants with masked hypertension to participants with sustained normotension, the third model included systolic office BP to account for the differences observed in this variable between the two groups.
Pulse wave velocity (PWV) is presented as the mean and 95% CI according to blood pressure classification; coronary artery calcium score (CACS) and carotid artery plaques are presented as the odds ratio (OR) and 95% CI for participants with masked hypertension compared with sustained normotension.
BP, blood pressure; CACS, coronary artery calcium score; OR, odds ratio; PWV, pulse wave velocity.
[a]Calculated based on 1963 (70%) of all 2806 participants with masked hypertension or sustained normotension.
[b]Calculated based on 2746 (97.9%) of all 2806 participants with masked hypertension or sustained normotension. Of these, 211 (7.7%) had CACS ≥100.
[c]Calculated based on 2806 (100%) of all 2806 participants with masked hypertension or sustained normotension. Of these, 1359 (48.4%) had carotid artery plaques ≥1.

participants with known antihypertensive treatment, which has previously been shown to have a higher prevalence of masked hypertension [9,10,13]. However, a previous study of only those without known hypertension reported a masked hypertension prevalence of 10% [28]. A majority of participants in our study with masked hypertension were men, which is in alignment with previous findings [9]. For office and home BP, we used the same BP monitoring intervals and devices, validated by the European Society of Hypertension (ESH), and adhered to current HBPM

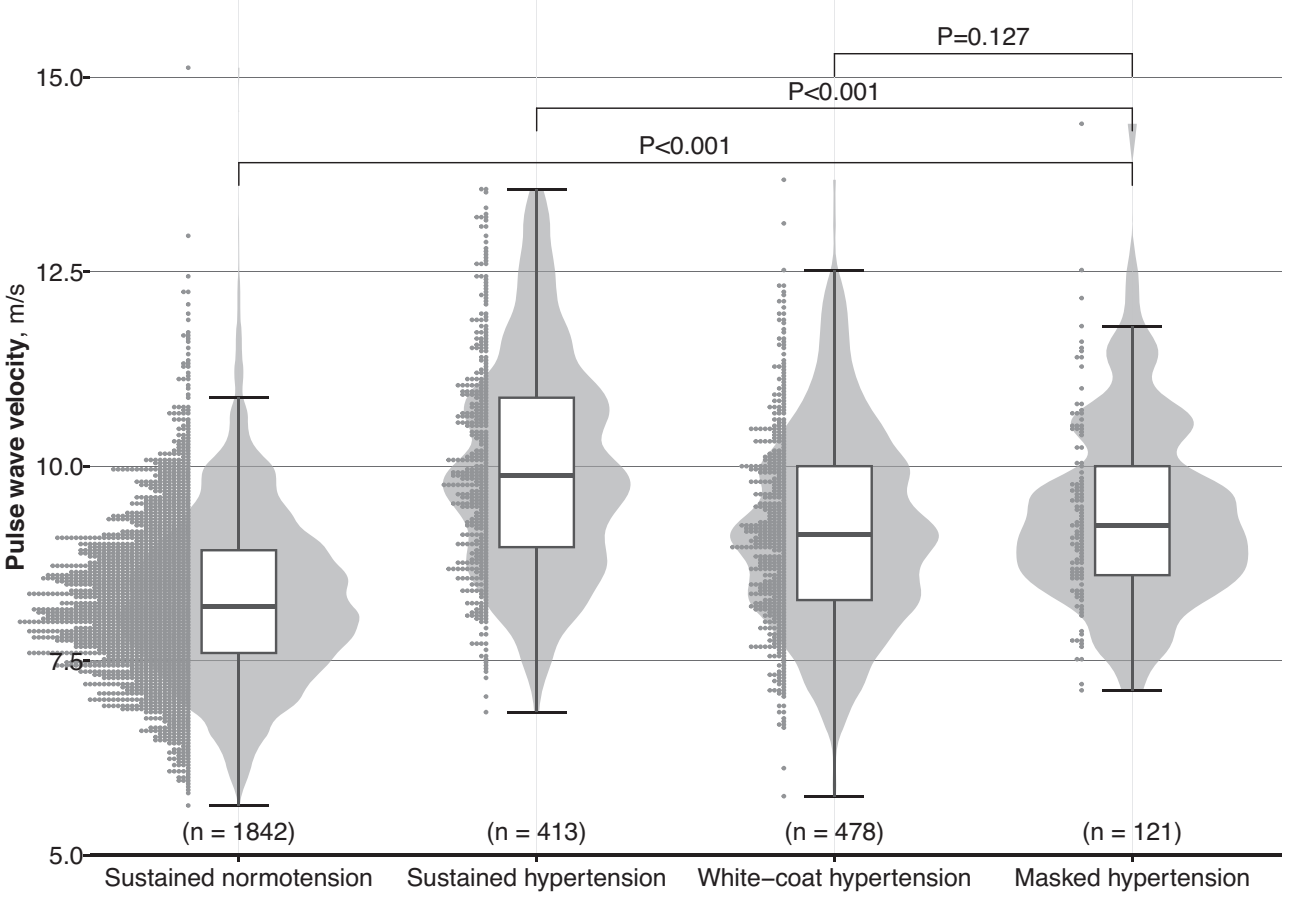

FIGURE 1 A box plot of pulse wave velocity in masked hypertension compared with sustained normotension, white-coat hypertension and sustained hypertension respectively. The boxplot includes the median, the box extending between the 25th to the 75th percentile (the interquartile range, IQR) and its whiskers extending between the IQR times 1.5; the violin plot illustrates the relative distribution of observations; and the left-sided vertical bar plot shows the actual observations.

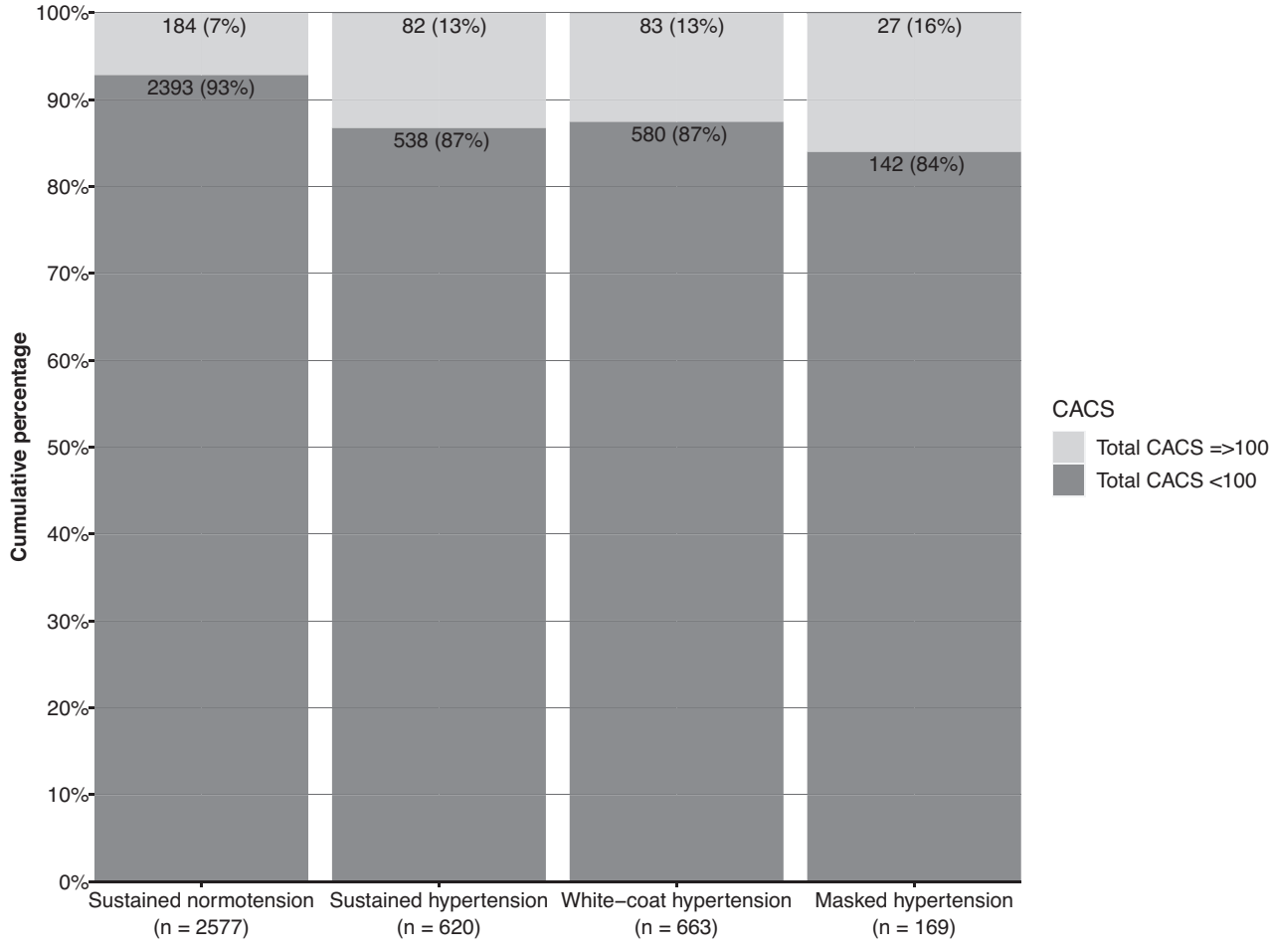

FIGURE 2 A cumulative bar plot of categorized coronary artery calcium score (CACS) in sustained normotension, sustained hypertension, white-coat hypertension and masked hypertension respectively. CACS, coronary artery calcium score.

monitoring recommendations [2,29]. To the best of our knowledge, this has not been previously achieved in such a large randomly selected cohort. Of participants, only two had less than the three morning and three evening registrations of HBPM advised by the current ESH recommendations [2].

Our study has some limitations. The participation rate was 58%, which could indicate self-selection, thus affecting the representativeness of the study sample. The SCAPIS pilot study found an association between choosing not to participate in the study and a lower socioeconomic status. However, the proportion of individuals with previous CVD or diabetes mellitus did not differ between participants and nonparticipants [30]. The missing rate for PWV was 30.0%, compared with an otherwise low missing rate of less than 2.2% for all other variables, because PWV analysis was performed only if time permitted after the biomedical scientist had performed echocardiography, which was prioritized. A potential weakness was also that office BP was measured in the supine position, while HBPM was measured in the sitting position. In Sweden, it is standard procedure to measure office BP in the supine position. A Swedish study found that the SBP was on average 1.2 mmHg lower when measured in the supine vs. the sitting position, although not in those aged 60–64 years [31]. However, other studies have found conflicting results, and that individual differences can be considerably larger than those at group level [32,33]. Such differences could have caused misclassification of hypertension phenotypes in our study. Current medications were reported by patients themselves rather than evaluated through register data, which is a potential source of inaccuracy. Finally, our study is cross-sectional, and causality can thus not be determined. However, the novel associations between masked hypertension and markers of CVD found in our study, based on a comparatively large sample size, emphasize the importance to evaluate patients with CVD and normotension at the office with HBPM.

In conclusion, participants with masked hypertension had increased markers of CVD when compared with participants that had normal BP at home. This clearly suggests that home BP is a better predictor of risk than office BP, even when the BP recordings are performed with the same device, in a population-based setting with randomized recruitment. Future prospective randomized trials to study how individuals with masked hypertension should be treated to reduce the risk for CVD, would hence be of great interest.

TABLE 3. Markers of cardiovascular disease in participants with masked hypertension compared with white-coat hypertension

	Model 1 (crude)		Model 2 (adjusted for age and sex)		Model 3 (adjusted for age, sex, fasting glucose and BMI)	
	Mean (95% CI)	*P*	Mean (95% CI)	*P*	Mean (95% CI)	*P*
Pulse wave velocity (m/s)						
White-coat hypertension	9.2 (9.1–9.3)	–	9.2 (9.0–9.4)	–	9.2 (9.0–9.4)	–
Masked hypertension	9.4 (9.2–9.6)	0.092	9.4 (9.1–9.6)	0.160	9.4 (9.1–9.6)	0.143
	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*
CACS ≥100	1.33 (0.83–2.13)	0.237	1.14 (0.70–1.87)	0.595	1.14 (0.69–1.88)	0.601
Carotid artery plaques ≥1	0.91 (0.65–1.28)	0.579	0.92 (0.65–1.31)	0.659	0.92 (0.65–1.31)	0.648

Values for pulse wave velocity (PWV), carotid artery calcium score (CACS) and carotid artery plaques were calculated based on 599 (70.1%), 832 (97.3%) and 855 (100%), respectively, of all 855 participants with white-coat hypertension or masked hypertension. PWV was calculated using a correction factor of 0.8 in accordance with current international guidelines [21]. Differences between means were tested using linear regression, and differences between odds ratios were tested using a generalized linear model.
Pulse wave velocity (PWV) is presented as the mean and 95% CI according to blood pressure classification; coronary artery calcium score (CACS) and carotid artery plaques are presented as the odds ratio (OR) and 95% CI for participants with masked hypertension compared with white coat hypertension.
CACS, coronary artery calcium score; OR, odds ratio; PWV, pulse wave velocity.

TABLE 4. Markers of cardiovascular disease in participants with masked hypertension compared with sustained hypertension

	Model 1 (crude)		Model 2 (adjusted for age and sex)		Model 3 (adjusted for age, sex, fasting glucose and BMI)	
	Mean (95% CI)	*P*	Mean (95% CI)	*P*	Mean (95% CI)	*P*
Pulse wave velocity (m/s)						
Sustained hypertension	10.0 (9.9–10.1)	–	10.0 (9.8–10.2)	–	10.0 (9.7–10.2)	–
Masked hypertension	9.4 (9.2–9.6)	<0.001	9.4 (9.2–9.6)	<0.001	9.3 (9.1–9.6)	<0.001
	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*
CACS ≥100	1.25 (0.78–2.00)	0.359	1.31 (0.81–2.13)	0.271	1.42 (0.87–2.32)	0.160
Carotid artery plaques ≥1	0.77 (0.55–1.09)	0.143	0.79 (0.56–1.12)	0.186	0.78 (0.55–1.10)	0.157

Values for pulse wave velocity (PWV), carotid artery calcium score (CACS) and carotid artery plaques were calculated based on 534 (66.3%), 789 (98%) and 805 (100%), respectively, of all 805 participants with sustained hypertension or masked hypertension. PWV was calculated using a correction factor of 0.8 in accordance with current international guidelines [21]. Differences between means were tested using linear regression, and differences between odds ratios were tested using a generalized linear model.
Pulse wave velocity is presented as the mean and 95% CI according to blood pressure classification; coronary artery calcium score (CACS) and carotid artery plaques are presented as the odds ratio (OR) and 95% CI for participants with masked hypertension compared with sustained hypertension.
CACS, coronary artery calcium score; OR, odds ratio; PWV, pulse wave velocity.

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Conflicts of interest

There are no conflicts of interest.

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