Relationship of Office and Ambulatory Blood Pressure With Left Ventricular Global Longitudinal Strain

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BACKGROUND
Left ventricular (LV) global longitudinal strain (GLS) is an early indicator of subclinical cardiac dysfunction, even when LV ejection fraction (LVEF) is normal, and is an independent predictor of cardiovascular events. Ambulatory blood pressure (BP) is a better predictor of cardiovascular events, including heart failure, than office BP. We investigated the association of office and ambulatory BP measurements with subclinical LV systolic dysfunction in a community-based cohort with normal LVEF.

METHODS
Two-dimensional speckle-tracking echocardiography and 24-hour ambulatory BP monitoring were performed in 577 participants (mean age 70 ± 9 years; 60% women) with LVEF ≥50% from the Cardiovascular Abnormalities and Brain Lesions (CABL) study. Univariable and multivariable linear regression analyses were used to assess the associations of BP measures with GLS.

RESULTS
Higher ambulatory and office BP values were consistently associated with impaired GLS. After adjustment for pertinent covariates (age, sex, race/ethnicity, body mass index, diabetes mellitus, coronary artery disease, LV mass index, and antihypertensive medication), office diastolic BP and ambulatory systolic and diastolic BPs (24-hour, daytime and nighttime) were independently associated with GLS ($P = 0.003$ for office DBP, $P \leq 0.001$ for all ambulatory BPs). When ambulatory and office BP values were included in the same model, all ambulatory BP measures remained significantly associated with GLS (all $P < 0.01$), whereas office BP values were not.

CONCLUSIONS
Ambulatory BP values are significantly associated with impaired GLS and the association is stronger than for office BP. Ambulatory BP monitoring might have a role in the risk stratification of hypertensive patients for early LV dysfunction.

Keywords: blood pressure; ambulatory blood pressure monitoring; echocardiography; hypertension; left ventricular function; longitudinal strain.

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The prevention of heart failure (HF) is an important public health goal, because HF has high prevalence, morbidity, mortality, and associated cost of care.[1–3] Early identification and aggressive management of patients at high risk of developing HF have been strongly recommended and may be of particular importance in the elderly patients, who are at highest risk of developing HF.[4,5] Hypertension is one of the most common precursors of HF, and elevated blood pressure (BP) is an important and modifiable risk factor for its development.[6,7] Ambulatory BP monitoring provides information that cannot be obtained from office BP measurements, such as nighttime and daytime mean values and circadian variability. Several epidemiological and clinical studies have demonstrated that ambulatory BP is a better predictor of adverse cardiovascular outcomes than office BP.[8,9]

Left ventricular (LV) global longitudinal strain (GLS) is an echocardiographic measure of LV systolic function and an indicator of early subclinical cardiac dysfunction, even when LV ejection fraction (LVEF) is in the normal range. Moreover, several studies have reported that GLS is a prognostic indicator for mortality, cardiovascular events, and HF development, independent of LVEF.[10–12] Recently, Ye *et al.* reported that higher pulsatile arterial load, and especially proximal arterial stiffness, was associated with impaired GLS, and that BP measures failed to show an independent association with GLS; however, ambulatory BP measures were not tested in that study.[13] Previous studies reported that ambulatory BP

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was more closely associated with echocardiographic parameters of LV hypertrophy and LV filling than office BP.[14,15] However, the association of ambulatory BP with subclinical LV systolic dysfunction detected by GLS has not been extensively studied. Furthermore, it is not known whether ambulatory BP measurements are more closely associated with LV subclinical dysfunction than office BP, and could therefore be used to as a predictor of LV subclinical dysfunction in hypertensive patients. Therefore, we investigated the association of office and ambulatory BP measurements with GLS in a community-based, predominantly elderly cohort with normal LVEF.

METHODS

Study population

The study cohort was derived from the Cardiovascular Abnormalities and Brain Lesions (CABL) study, whose participants were drawn from the Northern Manhattan Study (NOMAS). NOMAS is a population-based study designed to evaluate the incidence, risk factors, and clinical outcome of stroke in the population of northern Manhattan. Study design and the methodologies of NOMAS have previously been described in detail.[16] Briefly, subjects were eligible if they (i) had never been diagnosed with a stroke, (ii) were ≥40 years of age, and (iii) resided for at least 3 months in a household with a telephone in northern Manhattan. Beginning in September 2005, NOMAS subjects older than 50 years who voluntarily agreed to undergo a brain magnetic resonance imaging study and more extensive cardiovascular assessments were included in the CABL study, which was designed to investigate the relationship between subclinical cardiovascular disease and subclinical brain disease. Participants in CABL who had a complete dataset of 24-hour ambulatory BP monitoring and speckle-tracking strain imaging constitute the cohort of the present report. Subjects with LVEF <50% were excluded from the analysis.

The study was approved by the institutional review boards of Columbia University Medical Center and the University of Miami. Written informed consent was obtained from all study participants.

Risk factor assessment

Cardiovascular risk factors were ascertained through direct examination and interview by trained research assistants. Diabetes mellitus was defined by the patient's self-report, current use of insulin or hypoglycemic agents, or a fasting blood glucose ≥126 mg/dl on ≥2 occasions. Hypercholesterolemia was defined as total serum cholesterol >240 mg/dl, a patient's self-report of hypercholesterolemia or the use of lipid-lowering medication. Smoking status was defined as self-reported cigarette smoking at any time in the past or present. Body mass index was calculated as: weight/(height)^2 and expressed in kg/m^2. Coronary artery disease was defined as a history of myocardial infarction, coronary artery bypass grafting, or percutaneous coronary intervention.

Assessment of office BP and 24-hour ambulatory BP

Office systolic BP (SBP) and diastolic BP (DBP) were measured on the nondominant arm in a sitting position after 5 minutes of rest, using a mercury sphygmomanometer and an appropriate size arm cuff. Two BP measurements obtained after an interval of 5 minutes during the same visit were performed and averaged. Ambulatory BP monitoring was performed with an appropriately sized BP cuff on the nondominant arm, using a BP monitor (SpaceLabs Model 90207; Snoqualmie, WA) previously validated by the British Hypertension Society Protocol[17] and calibrated against a reference mercury sphygmomanometer. The methods of ambulatory BP monitoring have been previously published.[18] Briefly, the participants were asked to follow their usual routine and to note their activities at the time of each BP reading in a diary, as well as their sleep onset and wake-up times. A BP reading was automatically taken and recorded every 15 minutes during waking hours and every 30 minutes during sleeping hours for 24 hours. The mean SBP and DBP were calculated for the 24-hour period and separately for daytime (awake) and nighttime (sleep) periods, defined by subjects' diary reports of actual asleep and awake times. BP variability was defined as the SDs of mean BP, and calculated separately for daytime and nighttime. Night-to-day-ratios (nighttime BP/daytime BP) for SBP and DBP were also calculated. Non-dipping pattern was defined as SBP night-to-day ratio >0.9.

Echocardiographic assessment

Two-dimensional echocardiography. Transthoracic echocardiography was performed by trained registered sonographers, following a standardized protocol with a commercially available system (iE 33; Philips, Andover, MA). Interventricular septum and posterior wall thickness, LV end-diastolic and end-systolic diameters were measured from a parasternal long-axis view according to the recommendations of the American Society of Echocardiography.[19] LVEF was calculated using the biplane modified Simpson's rule. LV mass was calculated using the Devereux formula[20] and indexed by body surface area (LVMI).

Peak velocities of the early phase (E) of the mitral inflow were obtained by pulsed-wave Doppler at the mitral valve leaflet tips from an apical 4-chamber view. LV myocardial velocities by tissue Doppler imaging were obtained at the lateral and septal mitral valve annulus. The peak early diastolic (e') velocity was measured and the E/e' ratio was calculated as an index of LV filling pressure.

Speckle-tracking GLS imaging. Speckle-tracking analysis was performed off-line using commercially available software (QLAB Advanced Quantification Software version 8.1, Philips). GLS was calculated from the apical 4-chamber and 2-chamber views as previously described.[12,21] At least 2 cardiac cycles were recorded at a frame rate ≥45 fps, and were averaged for GLS analysis. Reproducibility of speckle-tracking measurements has been reported previously.[22]

Statistical analysis

Data are presented as mean ± SD for continuous variables and as proportions for categorical variables. Univariable linear regression analysis was used to assess the association of each BP measure with LVMI, *E/e′* and GLS. Multivariable linear regression analysis was performed separately for each ambulatory and office BP measure to assess their independent association with the echocardiographic parameters after adjustment for pertinent covariates, which were selected based on their bivariate association with each echocardiographic parameter (the threshold for inclusion in the multivariable models was set at a *P* value of <0.2). To examine whether ambulatory BP measures are more closely associated with the echocardiographic parameters than office BP, corresponding ambulatory and office BP variables were included in the same regression model. A *P* value of <0.05 was considered statistically significant. Statistical analyses were performed using SAS software version 9.3 (SAS, Cary, NC).

RESULTS

Study population

Of the 1,004 subjects enrolled in CABL, 835 had ambulatory BP monitoring performed. Of these, 604 had diagnostically adequate speckle-tracking GLS imaging available. Among those, 27 participants with LVEF <50% were excluded. Therefore, the final sample size of the present study consisted of 577 participants. The clinical and demographic characteristics of the study population are shown in Table 1. Almost 70% of the participants were taking antihypertensive medications.

Table 2 shows the association of LVMI, *E/e′* and GLS with demographics, risk factors and echocardiographic variables. Impaired (i.e., less negative) GLS was significantly associated with older age, diabetes mellitus, coronary artery disease, greater LV mass index (all $P < 0.01$), and antihypertensive medication use ($P < 0.05$).

Table 1. Characteristics of the study population

***N* = 577**	
Age, years	70.2 ± 9.1
Male	229 (39.7)
Race/ethnicity	
White	74 (12.8)
Black	96 (16.6)
Hispanic	398 (69.0)
Other	9 (1.6)
Body mass index, kg/m^2	27.8 ± 4.5
Antihypertensive medication use	394 (68.3)
Diabetes mellitus	166 (28.8)
Hypercholesterolemia	381 (66.0)
Smoking history	306 (53.0)
Coronary artery disease	34 (5.9)
Echocardiographic data	
LV septal thickness, mm	11.3 ± 1.7
LV end-diastolic dimension, mm	44.4 ± 4.2
LV posterior wall thickness, mm	11.0 ± 1.5
LV mass index, g/m^2	100.6 ± 23.7
LVEF, %	64.4 ± 4.9
E/e′	9.93 ± 4.25
GLS, %	−17.3 ± 3.0
Office and ambulatory BP values	
Office SBP, mm Hg	134.8 ± 16.6
Office DBP, mm Hg	78.5 ± 9.2
24-hour SBP, mm Hg	124.6 ± 14.1
24-hour DBP, mm Hg	71.4 ± 8.3

Values are shown as mean ± SD or *n* (%).

Abbreviations: LV, left ventricular; EF, ejection fraction; GLS, global longitudinal strain; *E*, early diastolic mitral inflow velocity; *e′*, early diastolic mitral annular tissue velocity; BP, blood pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure.

Association of BP measures with GLS

The association of various BP measurements with echocardiographic parameters (LVMI, *E/e′* and GLS) is summarized in Table 3. In univariate linear regression analyses examining each predictor in separately, all office BP and ambulatory BP measures showed significant association with GLS, except the night-to-day ratios, nighttime DBP variability, and non-dipping pattern. Similarly, LVMI showed a significant association with office and ambulatory BP values, except for office DBP. *E/e′* showed a significant association with BP night-to-day ratios and daytime DBP as well as with office and ambulatory SBP and SBP variability. Higher BP, both from office and ambulatory measurements, and greater BP variability were consistently associated with greater LVMI and impaired GLS. Higher night-to-day ratios, non-dipping pattern, and lower daytime DBP were significantly associated with higher *E/e′*. After adjustment (for age, sex, race/ethnicity, body mass index, diabetes mellitus, coronary artery disease, LV mass index, and antihypertensive medication use), office DBP and ambulatory 24-hour, daytime, and nighttime SBP and DBP remained significantly associated with GLS, whereas office SBP was no longer associated. Greater variability in nighttime SBP and daytime DBP also remained significantly associated with impaired GLS; however, neither variable remained independently associated with GLS when the corresponding average ambulatory BP value (nighttime SBP and daytime DBP) was simultaneously included in the regression model. After adjustment for relevant covariates, both ambulatory SBP and DBP remained significantly associated with LVMI, unlike office SBP and DBP. *E/e′* was only associated with ambulatory 24-hour, daytime and nighttime SBP. Night-to-day ratios and non-dipping pattern were no longer associated with *E/e′* in the multivariable analysis.

Table 2. Factors associated with LV mass index, *E*/*e*′ and GLS

	LV mass index		*E*/*e*′		GLS	
	B (SE)	*P* value	B (SE)	*P* value	B (SE)	*P* value
Age (per year)	0.41 (0.11)	<0.01	0.10 (0.01)	<0.01	0.05 (0.01)	<0.01
Male	5.30 (2.00)	0.01	−0.87 (0.24)	<0.01	0.45 (0.25)	0.07
Race/ethnicity		0.11		0.01		0.07
White	Reference		Reference		Reference	
Black	−6.39 (3.65)	0.08	1.37 (0.44)	<0.01	0.67 (0.46)	0.15
Hispanic	−1.20 (2.99)	0.69	0.73 (0.36)	0.04	−0.11 (0.38)	0.77
Other	−12.7 (8.33)	0.13	−0.33 (0.99)	0.74	−0.35 (1.05)	0.74
Body mass index (per kg/m^2)	0.06 (0.22)	0.77	0.05 (0.03)	0.04	0.04 (0.03)	0.19
Antihypertensive medication use	8.49 (2.09)	<0.01	1.44 (0.25)	<0.01	0.53 (0.27)	<0.05
Diabetes mellitus	5.41 (2.17)	0.01	0.95 (0.26)	<0.01	0.79 (0.27)	<0.01
Hypercholesterolemia	2.11 (2.08)	0.31	0.71 (0.25)	<0.01	0.33 (0.26)	0.20
Smoking history	−0.70 (1.98)	0.72	−0.30 (0.24)	0.20	0.16 (0.25)	0.51
Coronary artery disease	3.68 (4.18)	0.38	1.13 (0.51)	0.03	1.38 (0.52)	<0.01
LV end-diastolic dimension (per mm)	2.88 (0.20)	<0.01	−0.04 (0.03)	0.18	−0.002 (0.03)	0.95
LV mass index (per g/m^2)			0.02 (0.01)	<0.01	0.02 (0.01)	<0.01

Each row is evaluated separately.
Abbreviations: *E*, early diastolic mitral inflow velocity; *e*′, early diastolic mitral annular tissue velocity; GLS, global longitudinal strain; B, parameter estimate; LV, left ventricular.

Relationship of GLS to ambulatory BP and office BP

When ambulatory SBP and office SBP, or ambulatory DBP and office DBP, were entered in the same multivariable model, both ambulatory SBP and DBP remained significantly associated with GLS in any of the 24-hour, daytime, and nighttime periods, whereas office SBP and DBP no longer showed a significant association with GLS (Table 4). The significant association of ambulatory SBP and DBP with LVMI remained even after an additional adjustment for each corresponding office BP value (Table 4). Ambulatory SBP (24-hour, daytime, and nighttime) remained significantly associated with *E*/*e*′.

DISCUSSION

In this community-based, predominantly elderly cohort, we demonstrated that (i) office DBP and ambulatory SBP and DBP in any of the 24-hour, daytime, and nighttime periods were significantly associated with GLS independently of cardiovascular risk factors; (ii) ambulatory SBP and DBP, but not office BP, were significantly associated with LVMI, whereas only ambulatory SBP was associated with *E*/*e*′ after adjustment for demographics and potential confounders; and (iii) ambulatory BP contributed more to explaining the variance of GLS as well as LVMI and *E*/*e*′ than office BP.

Previous studies have reported that ambulatory BP was more closely associated with echocardiographic parameters of LV hypertrophy and LV filling pressure than office BP, a circumstance that is in accordance with our findings.[14,15,23] Several clinical studies in selected populations with little concomitant disease previously reported that systolic longitudinal strain derived from two-dimensional speckle-tracking echocardiography was significantly impaired in hypertensive subjects, as well as in subjects with high-normal BP, compared with normotensive control subjects.[24–26] However, 1 study reported that significantly impaired GLS was observed only in hypertensive patients with extreme LV hypertrophic remodeling (LV mass >190 g).[27] In the present study, we demonstrate in a larger sample a significant association between higher BP values, except for office SBP, and impaired GLS even after adjustment for possible confounders, including diabetes mellitus, coronary artery disease, and LVMI. Furthermore, we demonstrate for the first time that ambulatory BP values are more closely associated with GLS than office BP measurements. Higher ambulatory BP was significantly associated with impaired GLS after adjustment for pertinent covariates and also for office BP, whereas office BP was no longer associated with GLS after adjustments for covariates. Ambulatory BP monitoring allows multiple BP measurements outside of the hospital, which are free from observer bias and white coat effect, and provides more reproducible information than office BP measurements.[28,29] In fact, marked discrepancies have been documented between office and ambulatory BP measurements.[30] From our results, ambulatory BP monitoring appears to be of value for the identification of subjects at risk of subclinical LV systolic dysfunction, who are at risk of adverse events.[10–12] Our findings are consistent with previous studies, in which target organ damage and adverse cardiovascular outcomes were more strongly associated with ambulatory BP than with office BP.[8,9,31,32]

Hypertension is a major risk factor for HF, not only because it increases the risk of coronary artery disease, but

Table 3. Association of blood pressure measures with LVmass index, *E*/*e*′, and GLS

	Unadjusted			Adjusted		
Predictor	**LVMI**	***E*/*e*′**	**GLS**	**LVMI[a]**	***E*/*e*′[b]**	**GLS[c]**
Office SBP (per mm Hg)	0.25 (0.06)‡	0.02 (0.01)†	0.02 (0.01)†	0.09 (0.05)	−0.002 (0.007)	0.01 (0.01)
24-hour SBP (per mm Hg)	0.55 (0.07)‡	0.05 (0.01)‡	0.05 (0.01)‡	0.37 (0.06)‡	0.03 (0.01)†	0.04 (0.01)‡
Daytime SBP (per mm Hg)	0.54 (0.07)‡	0.05 (0.01)‡	0.05 (0.01)‡	0.36 (0.06)‡	0.03 (0.01)†	0.04 (0.01)‡
Nighttime SBP (per mm Hg)	0.43 (0.06)‡	0.04 (0.01)‡	0.04 (0.01)‡	0.29 (0.05)‡	0.02 (0.01)†	0.03 (0.01)†
SBP night-to-day ratio (per %)	17.7 (13.5)	4.54 (1.61)†	1.52 (1.70)	6.73 (11.3)	0.56 (1.53)	−0.50 (1.70)
Daytime SBP variability (per mm Hg)	0.89 (0.30)†	0.14 (0.04)‡	0.09 (0.04)*	0.44 (0.26)	0.01 (0.04)	0.04 (0.04)
Daytime SBP variability (per mm Hg)[d]				0.05 (0.26)	−0.01 (0.04)	−0.001 (0.04)
Nighttime SBP variability (per mm Hg)	0.75 (0.30)*	0.09 (0.04)*	0.12 (0.04)†	0.30 (0.25)	0.01 (0.03)	0.09 (0.04)*
Nighttime SBP variability (per mm Hg)[d]				−0.01 (0.25)	−0.01 (0.04)	0.07 (0.04)
Office DBP (per mm Hg)	0.06 (0.11)	−0.01 (0.01)	0.04 (0.01)†	0.08 (0.09)	−0.02 (0.01)	0.04 (0.01)†
24-hour DBP (per mm Hg)	0.39 (0.12)†	−0.02 (0.01)	0.08 (0.01)‡	0.53 (0.10)‡	−0.004 (0.01)	0.08 (0.02)‡
Daytime DBP (per mm Hg)	0.36 (0.11)†	−0.03 (0.01)*	0.07 (0.01)‡	0.52 (0.10)‡	−0.01 (0.01)	0.08 (0.01)‡
Nighttime DBP (per mm Hg)	0.31 (0.11)†	0.01 (0.01)	0.06 (0.01)‡	0.35 (0.09)‡	0.01 (0.01)	0.06 (0.01)‡
DBP Night-to-day ratio (per %)	2.43 (12.0)	5.02 (1.44)†	1.08 (1.51)	−7.84 (10.1)	2.48 (1.36)	−0.24 (1.52)
Daytime DBP variability (per mm Hg)	1.09 (0.43)*	0.03 (0.05)	0.17 (0.05)†	0.94 (0.36)†	−0.07 (0.05)	0.14 (0.05)*
Daytime DBP variability (per mm Hg)[d]				0.63 (0.36)	−0.07 (0.05)	0.09 (0.05)
Nighttime DBP variability (per mm Hg)	−0.18 (0.42)	−0.06 (0.05)	0.04 (0.05)	−0.35 (0.34)	−0.06 (0.05)	0.04 (0.05)
Nighttime DBP variability (per mm Hg)[d]				−0.49 (0.34)	−0.06 (0.05)	0.01 (0.05)
Non-dipping pattern[e]	0.0005 (2.02)	0.70 (0.24) †	0.17 (0.25)	−1.88 (1.68)	0.27 (0.23)	0.001 (0.25)

Values are parameter estimates (B) and SE. Each predictor is evaluated in a separate model. *$P < 0.05$, †$P < 0.01$, ‡$P < 0.001$.

Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; LVMI, left ventricular mass index; *E*, early diastolic mitral inflow velocity; *e*′, early diastolic mitral annular tissue velocity; GLS, global longitudinal strain.

[a]Adjusted for age, sex, race/ethnicity, diabetes mellitus, LV end-diastolic dimension, and antihypertensive medication use.

[b]Adjusted for age, sex, race/ethnicity, body mass index, diabetes mellitus, hypercholesterolemia, coronary artery disease, LV end-diastolic dimension, LV mass index, and antihypertensive medication use.

[c]Adjusted for age, sex, race/ethnicity, body mass index, diabetes mellitus, coronary artery disease, LV mass index, and antihypertensive medication use.

[d]In addition to the general adjustments, data were further adjusted for the corresponding mean ambulatory BP value.

[e]Defined as SBP night-to-day ratio >0.9.

also because elevated BP directly induces pressure-overload, which leads to LV hypertrophy with associated interstitial and perivascular fibrosis.[33,34] GLS is mainly a measure of the contraction of the longitudinally oriented myocardial fibers, which are mostly located in the LV subendocardium. In a hypertensive animal model, the elevation of wall stress, accumulation of fibrosis, and myocyte hypertrophy were distributed predominantly in the LV subendocardium, and the impairment of GLS occurred in parallel with fibrosis in the early stage of hypertensive HF.[35] In our study, higher ambulatory BP showed a significant association with impaired GLS that was independent of LV mass. Therefore, we speculate that GLS may be impaired in hypertension not only as a result of LV hypertrophy, but also because of a direct effect of increased LV afterload, and that ambulatory BP measurements may provide more accurate information on LV pressure-overload than office BP. Assessing BP status by ambulatory monitoring rather than office BP may help identify subjects at risk of subclinical LV dysfunction, to whom aggressive treatment could be aimed to decrease the likelihood of progression toward clinical systolic dysfunction.

Our study has several limitations. The cross-sectional design does not allow us to detect causal relationships; prospective investigation would be necessary to assess whether ambulatory BP values can predict the future development of subclinical LV dysfunction. The assessment of relative importance of office and ambulatory BP values in the same model can be substantially sample-dependent due to multicollinearity of ambulatory and office BP. However, the beta estimates we presented can be directly interpreted as the change that occurs when each of the relevant variables is added to the same model. Furthermore, despite being representative of the multiethnic community living in northern Manhattan, our cohort is predominantly elderly and has a high frequency of cardiovascular risk factors; therefore the results of the present study might not be directly applicable to other populations with different demographics and risk factor distribution. Finally, our cohort had a high rate of antihypertensive medication use; although antihypertensive

Table 4. Association of office BP and ambulatory BP with LV mass index, *E*/*e*′, and GLS

	LVMI[a]		*E*/*e*′[b]		GLS[c]	
Model	**B (SE)**	***P* value**	**B (SE)**	***P* value**	**B (SE)**	***P* value**
Office SBP + 24-hour SBP						
Office SBP	−0.01 (0.05)	0.81	−0.009 (0.008)	0.22	0.003 (0.01)	0.73
24-hour SBP	0.37 (0.06)	<0.0001	0.04 (0.01)	<0.0001	0.04 (0.01)	0.0002
Office SBP + daytime SBP						
Office SBP	−0.009 (0.05)	0.87	−0.009 (0.008)	0.24	0.003 (0.01)	0.73
Daytime SBP	0.36 (0.06)	<0.0001	0.04 (0.01)	<0.0001	0.04 (0.01)	0.0001
Office SBP + nighttime SBP						
Office SBP	0.01 (0.05)	0.83	−0.007 (0.008)	0.34	0.006 (0.01)	0.49
Nighttime SBP	0.28 (0.06)	<0.0001	0.03 (0.01)	0.0002	0.03 (0.01)	0.003
Office DBP + 24-hour DBP						
Office DBP	−0.09 (0.10)	0.32	−0.03 (0.01)	0.04	0.02 (0.01)	0.21
24-hour DBP	0.57 (0.11)	<0.0001	0.02 (0.02)	0.19	0.07 (0.02)	<0.0001
Office DBP + daytime DBP						
Office DBP	−0.09 (0.09)	0.34	−0.03 (0.01)	0.07	0.02 (0.01)	0.19
Daytime DBP	0.56 (0.10)	<0.0001	0.01 (0.01)	0.43	0.07 (0.02)	<0.0001
Office DBP + nighttime DBP						
Office DBP	−0.03 (0.09)	0.74	−0.03 (0.01)	0.03	0.03 (0.01)	0.07
Nighttime DBP	0.36 (0.10)	0.0002	0.03 (0.01)	0.047	0.05 (0.01)	0.0008

Values are parameter estimates (B) and SE.

Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; LVMI, left ventricular mass index; *E*, early diastolic mitral inflow velocity; *e*′, early diastolic mitral annular tissue velocity; GLS, global longitudinal strain.

[a]Adjusted for age, sex, race/ethnicity, diabetes mellitus, LV end-diastolic dimension, and antihypertensive medication use.

[b]Adjusted for age, sex, race/ethnicity, body mass index, diabetes mellitus, hypercholesterolemia, coronary artery disease, LV end-diastolic dimension, LV mass index, and antihypertensive medication use.

[c]Adjusted for age, sex, race/ethnicity, body mass index, diabetes mellitus, coronary artery disease, LV mass index, and antihypertensive medication use.

treatment was adjusted for in the multivariable analyses, the results may not be directly applicable to a normotensive cohort.

In conclusion, in our community-based, predominantly elderly cohort, higher ambulatory BP was significantly associated with impaired GLS in subjects with normal LVEF, independently of cardiovascular risk factors. Moreover, the association of ambulatory BP with impaired GLS was stronger than office BP values. Ambulatory BP monitoring might have a role in the risk stratification of hypertensive patients for early LV dysfunction.

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DISCLOSURE

The authors declared no conflict of interest.

REFERENCES

1. Go AS, Mozaffarian D, Roger VL, Benjamin EJ, Berry JD, Blaha MJ, Dai S, Ford ES, Fox CS, Franco S, Fullerton HJ, Gillespie C, Hailpern SM, Heit JA, Howard VJ, Huffman MD, Judd SE, Kissela BM, Kittner SJ, Lackland DT, Lichtman JH, Lisabeth LD, Mackey RH, Magid DJ, Marcus GM, Marelli A, Matchar DB, McGuire DK, Mohler ER 3rd, Moy CS, Mussolino ME, Neumar RW, Nichol G, Pandey DK, Paynter NP, Reeves MJ, Sorlie PD, Stein J, Towfighi A, Turan TN, Virani SS, Wong ND, Woo D, Turner MB. Heart disease and stroke statistics--2014 update: a report from the American Heart Association. *Circulation* 2014; 129:e28–e292.
2. Heidenreich PA, Albert NM, Allen LA, Bluemke DA, Butler J, Fonarow GC, Ikonomidis JS, Khavjou O, Konstam MA, Maddox TM, Nichol G, Pham M, Pina IL, Trogdon JG. Forecasting the impact of heart failure in the United States: a policy statement from the American Heart Association. *Circ Heart Fail* 2013; 6:606–619.
3. Levy D, Kenchaiah S, Larson MG, Benjamin EJ, Kupka MJ, Ho KK, Murabito JM, Vasan RS. Long-term trends in the incidence of and survival with heart failure. *N Engl J Med* 2002; 347:1397–1402.
4. Schocken DD, Benjamin EJ, Fonarow GC, Krumholz HM, Levy D, Mensah GA, Narula J, Shor ES, Young JB, Hong Y. Prevention of heart

failure: a scientific statement from the American Heart Association Councils on Epidemiology and Prevention, Clinical Cardiology, Cardiovascular Nursing, and High Blood Pressure Research; Quality of Care and Outcomes Research Interdisciplinary Working Group; and Functional Genomics and Translational Biology Interdisciplinary Working Group. *Circulation* 2008; 117:2544–2565.
5. Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE Jr, Drazner MH, Fonarow GC, Geraci SA, Horwich T, Januzzi JL, Johnson MR, Kasper EK, Levy WC, Masoudi FA, McBride PE, McMurray JJ, Mitchell JE, Peterson PN, Riegel B, Sam F, Stevenson LW, Tang WH, Tsai EJ, Wilkoff BL. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. *Circulation* 2013; 128:e240–e327.
6. Levy D, Larson MG, Vasan RS, Kannel WB, Ho KK. The progression from hypertension to congestive heart failure. *JAMA* 1996; 275:1557–1562.
7. Rapsomaniki E, Timmis A, George J, Pujades-Rodriguez M, Shah AD, Denaxas S, White IR, Caulfield MJ, Deanfield JE, Smeeth L, Williams B, Hingorani A, Hemingway H. Blood pressure and incidence of twelve cardiovascular diseases: lifetime risks, healthy life-years lost, and age-specific associations in 1·25 million people. *Lancet* 2014; 383:1899–1911.
8. Hansen TW, Jeppesen J, Rasmussen S, Ibsen H, Torp-Pedersen C. Ambulatory blood pressure and mortality: a population-based study. *Hypertension* 2005; 45:499–504.
9. Clement DL, De Buyzere ML, De Bacquer DA, de Leeuw PW, Duprez DA, Fagard RH, Gheeraert PJ, Missault LH, Braun JJ, Six RO, Van Der Niepen P, O'Brien E. Prognostic value of ambulatory blood-pressure recordings in patients with treated hypertension. *N Engl J Med* 2003; 348:2407–2415.
10. Stanton T, Leano R, Marwick TH. Prediction of all-cause mortality from global longitudinal speckle strain: comparison with ejection fraction and wall motion scoring. *Circ Cardiovasc Imaging* 2009; 2:356–364.
11. Ersbøll M, Valeur N, Mogensen UM, Andersen MJ, Møller JE, Velazquez EJ, Hassager C, Søgaard P, Køber L. Prediction of all-cause mortality and heart failure admissions from global left ventricular longitudinal strain in patients with acute myocardial infarction and preserved left ventricular ejection fraction. *J Am Coll Cardiol* 2013; 61:2365–2373.
12. Russo C, Jin Z, Elkind MS, Rundek T, Homma S, Sacco RL, Di Tullio MR. Prevalence and prognostic value of subclinical left ventricular systolic dysfunction by global longitudinal strain in a community-based cohort. *Eur J Heart Fail* 2014; 16:1301–1309.
13. Ye Z, Coutinho T, Pellikka PA, Villarraga HR, Borlaug BA, Kullo IJ. Associations of alterations in pulsatile arterial load with left ventricular longitudinal strain. *Am J Hypertens* 2015; 28:1325–1331.
14. Cuspidi C, Lonati L, Sampieri L, Macca G, Valagussa L, Zaro T, Michev I, Salerno M, Leonetti G, Zanchetti A. Blood pressure control in a hypertension hospital clinic. *J Hypertens* 1999; 17:835–841.
15. Zhang Y, Kollias G, Argyris AA, Papaioannou TG, Tountas C, Konstantonis GD, Achimastos A, Blacher J, Safar ME, Sfikakis PP, Protogerou AD. Association of left ventricular diastolic dysfunction with 24-h aortic ambulatory blood pressure: the SAFAR study. *J Hum Hypertens* 2015; 29:442–448.
16. Sacco RL, Anand K, Lee HS, Boden-Albala B, Stabler S, Allen R, Paik MC. Homocysteine and the risk of ischemic stroke in a triethnic cohort: the NOrthern MAnhattan Study. *Stroke* 2004; 35:2263–2269.
17. O'Brien E, Mee F, Atkins N, O'Malley K. Accuracy of the SpaceLabs 90207 determined by the British Hypertension Society protocol. *J Hypertens* 1991; 9:573–574.
18. Iwata S, Jin Z, Schwartz JE, Homma S, Elkind MS, Rundek T, Sacco RL, Di Tullio MR. Relationship between ambulatory blood pressure and aortic arch atherosclerosis. *Atherosclerosis* 2012; 221:427–431.
19. Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, Picard MH, Roman MJ, Seward J, Shanewise JS, Solomon SD, Spencer KT, Sutton MS, Stewart WJ. Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. *J Am Soc Echocardiogr* 2005; 18:1440–1463.
20. Devereux RB, Alonso DR, Lutas EM, Gottlieb GJ, Campo E, Sachs I, Reichek N. Echocardiographic assessment of left ventricular hypertrophy: comparison to necropsy findings. *Am J Cardiol* 1986; 57:450–458.
21. Russo C, Jin Z, Homma S, Elkind MS, Rundek T, Yoshita M, DeCarli C, Wright CB, Sacco RL, Di Tullio MR. Subclinical left ventricular dysfunction and silent cerebrovascular disease: the Cardiovascular Abnormalities and Brain Lesions (CABL) study. *Circulation* 2013; 128:1105–1111.
22. Russo C, Jin Z, Homma S, Rundek T, Elkind MS, Sacco RL, Di Tullio MR. Relationship of multidirectional myocardial strain with radial thickening and ejection fraction and impact of left ventricular hypertrophy: a study in a community-based cohort. *Echocardiography* 2013; 30:794–802.
23. Mancia G, Zanchetti A, Agabiti-Rosei E, Benemio G, De Cesaris R, Fogari R, Pessina A, Porcellati C, Rappelli A, Salvetti A, Trimarco B. Ambulatory blood pressure is superior to clinic blood pressure in predicting treatment-induced regression of left ventricular hypertrophy. SAMPLE Study Group. Study on Ambulatory Monitoring of Blood Pressure and Lisinopril Evaluation. *Circulation* 1997; 95:1464–1470.
24. Miyoshi H, Oishi Y, Mizuguchi Y, Iuchi A, Nagase N, Ara N, Oki T. Effect of an increase in left ventricular pressure overload on left atrial-left ventricular coupling in patients with hypertension: a two-dimensional speckle tracking echocardiographic study. *Echocardiography* 2013; 30:658–666.
25. Di Bello V, Talini E, Dell'Omo G, Giannini C, Delle Donne MG, Canale ML, Nardi C, Palagi C, Dini FL, Penno G, Del Prato S, Marzilli M, Pedrinelli R. Early left ventricular mechanics abnormalities in prehypertension: a two-dimensional strain echocardiography study. *Am J Hypertens* 2010; 23:405–412.
26. Tadic M, Majstorovic A, Pencic B, Ivanovic B, Neskovic A, Badano L, Stanisavljevic D, Scepanovic R, Stevanovic P, Celic V. The impact of high-normal blood pressure on left ventricular mechanics: a three-dimensional and speckle tracking echocardiography study. *Int J Cardiovasc Imaging* 2014; 30:699–711.
27. Narayanan A, Aurigemma GP, Chinali M, Hill JC, Meyer TE, Tighe DA. Cardiac mechanics in mild hypertensive heart disease: a speckle-strain imaging study. *Circ Cardiovasc Imaging* 2009; 2:382–390.
28. O'Brien E, Parati G, Stergiou G, Asmar R, Beilin L, Bilo G, Clement D, de la Sierra A, de Leeuw P, Dolan E, Fagard R, Graves J, Head GA, Imai Y, Kario K, Lurbe E, Mallion JM, Mancia G, Mengden T, Myers M, Ogedegbe G, Ohkubo T, Omboni S, Palatini P, Redon J, Ruilope LM, Shennan A, Staessen JA, vanMontfrans G, Verdecchia P, Waeber B, Wang J, Zanchetti A, Zhang Y. European Society of Hypertension position paper on ambulatory blood pressure monitoring. *J Hypertens* 2013; 31:1731–1768.
29. Palatini P, Mormino P, Canali C, Santonastaso M, De Venuto G, Zanata G, Pessina AC. Factors affecting ambulatory blood pressure reproducibility. Results of the HARVEST Trial. Hypertension and Ambulatory Recording Venetia Study. *Hypertension* 1994; 23:211–216.
30. Lehmann MV, Zeymer U, Dechend R, Kaiser E, Hagedorn I, Deeg E, Senges J, Schmieder RE. Ambulatory blood pressure monitoring: is it mandatory for blood pressure control in treated hypertensive patients? Prospective observational study. *Int J Cardiol* 2013; 168:2255–2263.
31. Sega R, Trocino G, Lanzarotti A, Carugo S, Cesana G, Schiavina R, Valagussa F, Bombelli M, Giannattasio C, Zanchetti A, Mancia G. 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; 104:1385–1392.
32. Hara A, Tanaka K, Ohkubo T, Kondo T, Kikuya M, Metoki H, Hashimoto T, Satoh M, Inoue R, Asayama K, Obara T, Hirose T, Izumi S, Satoh H, Imai Y. Ambulatory versus home versus clinic blood pressure: the association with subclinical cerebrovascular diseases: the Ohasama Study. *Hypertension* 2012; 59:22–28.
33. Weber KT, Brilla CG. Pathological hypertrophy and cardiac interstitium. Fibrosis and renin-angiotensin-aldosterone system. *Circulation* 1991; 83:1849–1865.
34. Rossi MA. Pathologic fibrosis and connective tissue matrix in left ventricular hypertrophy due to chronic arterial hypertension in humans. *J Hypertens* 1998; 16:1031–1041.
35. Ishizu T, Seo Y, Kameda Y, Kawamura R, Kimura T, Shimojo N, Xu D, Murakoshi N, Aonuma K. Left ventricular strain and transmural distribution of structural remodeling in hypertensive heart disease. *Hypertension* 2014; 63:500–506.