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Arterial Stiffness is Associated with Increase in Blood Pressure Over Time in Treated Hypertensives

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Abstract

Background—Arterial stiffness is associated with incident hypertension. We hypothesized that arterial stiffness would predict increases in systolic (SBP), mean (MAP) and pulse pressure (PP) over time in treated hypertensives.

Methods—Blood pressure (BP) was measured a mean of 8.5±0.9 years apart in 414 non-Hispanic white hypertensives (mean age 60±8 years, 55% women). The average of 3 supine right brachial BPs was recorded. Measures of arterial stiffness including carotid-femoral pulse wave velocity (cfPWV), aortic augmentation index (AIx) and central pulse pressure (CPP) were obtained at baseline by applanation tonometry. We performed stepwise multivariable linear regression analyses adjusting for potential confounders to assess the associations of arterial stiffness parameters with BP changes over time.

Results—Systolic, mean and pulse pressure increased in 80% of participants. After adjustment for the covariates listed above, cfPWV was significantly associated with increases in SBP (β±SE: 0.71±0.31) and PP (β±SE: 1.09±0.27); AIx was associated with increases in SBP (β±SE: 0.23±0.10) and MAP (β±SE: 0.27±0.07); and CPP was associated with increases in SBP (β±SE: 0.44±0.07), MAP (β±SE: 0.24±0.05) and PP (β±SE: 0.42±0.06) over time ($P \leq 0.02$ for all).

Conclusions—Baseline arterial stiffness measures were associated with longitudinal increases in SBP, MAP and PP in treated hypertensives.

Keywords

hypertension; pulse wave velocity; pulse pressure; augmentation index

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Introduction

Hypertension is a major cause of morbidity in the United States, being associated with coronary artery disease,(1) stroke, (2) renal disease(3) and heart failure.(4) Hypertension affects 1 in 3 American adults, (5) and only 48% of those aware of their condition achieve optimal blood pressure (BP) control.(5) Even small increments in BP are clinically relevant, as a 2 mm Hg increase in systolic BP has been shown to be associated with a 7% increase in mortality from coronary artery disease and 10% increase in stroke mortality. (6) Moreover, the number of deaths attributable to hypertension increased by nearly 50% between 1998 and 2008,(5) highlighting the need for better strategies to identify and treat those at greater risk for worsening of hypertension and adverse outcomes.

In the past decade attention has focused on the associations of arterial stiffness with cardiovascular risk factors and adverse outcomes. The aorta not only functions as a conduit of blood, but also buffers the pulsatile energy generated by the heart with each cardiac cycle, thereby decreasing afterload and stroke work, and preventing the delivery of deleterious, highly pulsatile energy to the end-organs. As the aorta stiffens, there are greater swings in BP, pulse pressure increases, cardiac function is impaired and end-organ damage ensues.(7) As a result, arterial stiffness is independently associated with adverse cardiovascular events (8) and mortality,(9–11) and the European Societies of Cardiology and Hypertension have recommended assessment of arterial stiffness in all hypertensives for whom the technique is available.(12)

Given the deleterious effects of hypertension on cardiovascular health and survival, there is a need for markers that identify hypertensive individuals whose BPs are more likely to increase over time, so they can be treated more aggressively to reduce adverse outcomes. Greater aortic stiffness has been shown to be associated with incident hypertension and increases in BP over time in the general population. (13) Whether measures of arterial stiffness predict longitudinal changes in BP in treated hypertensive individuals remains unknown. To address this gap in knowledge, we studied a cohort of hypertensives from the general population to determine whether measures of arterial stiffness (carotid-femoral pulse wave velocity, aortic augmentation index and central pulse pressure) predict longitudinal changes in systolic, mean and pulse pressure.

Methods

Study participants

The study participants consisted of 414 hypertensive non-Hispanic white participants from the Genetic Epidemiology Network of Arteriopathy (GENOA) study (14,15) who underwent measurement of arterial stiffness on 2 separate occasions (between January 2003 and December 2008, and between October 2009 and December 2011). The GENOA study is community-based study aimed at identifying genetic variants influencing BP levels and the development of target-organ damage due to hypertension. Participants belong to sibships with at least 2 family members diagnosed with essential hypertension before the age of 60 years. The diagnosis of hypertension was established based on a prior diagnosis of hypertension and/or current treatment with medications for hypertension. The study was

approved by the Mayo Clinic's Institutional Review Board and participants gave informed consent.

Assessment of BP and baseline characteristics

On the day of the study, participants met with the study coordinator and completed a comprehensive questionnaire that included demographic, social, family and medical information. Brachial systolic (SBP) and diastolic blood pressures (DBP) were measured in the supine position by trained technicians 3 consecutive times with a random-zero sphygmomanometer, by auscultating at 2-min intervals, and their average was used for analyses. Mean brachial arterial pressure (MAP) was calculated as [(2 * DBP) + SBP] / 3. Brachial pulse pressure (PP) was calculated as brachial SBP – DBP.

A blood specimen was collected, and serum creatinine and glucose were measured by standard enzymatic methods. Glomerular filtration rate (GFR) was estimated based on the Modification of Diet in Renal Disease equation.(16) Diabetes was considered present if a subject was being treated with insulin or oral agents, or had a fasting glucose level ≥ 7.0 mmol/L (>126 mg/dL). 'Ever' smoking was defined as having smoked more than 100 cigarettes in the past. Weight (in kg) was measured by an electronic scale, height (in meters) by a stadiometer, and body mass index (BMI) was calculated in units of kg/m^2.

Arterial tonometry

We assessed 3 measures of arterial stiffness: carotid-femoral pulse wave velocity (cfPWV), considered the gold standard measure of aortic stiffness, aortic augmentation index (AIx), a measure of arterial wave reflection, and central pulse pressure (CPP), a global measure of arterial stiffness. Participants were asked to fast for 12 h and withhold vasoactive medications, alcohol and caffeine 24 h prior to the study visit. Arterial tonometry of the right carotid, radial and femoral arteries was performed at the time of the initial study visit using the Sphygmocor apparatus (AtCor Medical, Sydney, Australia) with simultaneous ECG recording as previously described.(17) Transit distances were obtained with the subtraction method from body surface measurements from the carotid sampling site to the manubrium sternum and from the manubrium sternum to the femoral artery. The time (t) between the onset of carotid and femoral waveforms was determined as the mean of 10 consecutive cardiac cycles. cfPWV was calculated from the distance between measurement points (D) and the measured time delay (t) as follows: cfPWV=D/t (m/s), where D is distance in meters and t is the time interval in seconds. An aortic pressure waveform was derived from the radial artery waveforms using a generalized transfer function.(18) From the derived aortic pressure waveform, CPP was calculated as the difference between central SBP and DBP. Aortic augmentation pressure was calculated as the difference between the first and second systolic peaks of the ascending aortic waveform, and AIx was expressed as a percentage of the CPP.

Statistical analyses

Continuous variables are reported as mean ± standard deviation (SD). Differences in BP parameters between the 1^{st} and 2^{nd} study visits were compared using a paired t-test. Categorical variables were reported as number (n) and percentages of the total (%).

Changes in BP (SBP, DBP, MAP and PP) over time were determined by calculating the difference between absolute values of BP components (BP at 2nd visit – BP at 1st visit). We developed multivariable linear regression models to assess the associations of baseline cfPWV, AIx and CPP with longitudinal changes in BP components. To account for relatedness among the participants, all regression models were performed using generalized estimating equations. Covariates considered for inclusion in the multivariate models were: age, sex, time interval between the 2 visits, baseline SBP and DBP, history of diabetes, smoking, myocardial infarction or stroke, BMI, GFR, use of statins and difference in the number of anti-hypertensive medications between 2nd and 1st visits. Only covariates significantly associated ($P \leq 0.05$) with the dependent variable were included in the final models, but age and sex were forced into all models. To determine whether age and sex modified the associations between arterial stiffness and hypertension progression, interaction terms for age, sex and each arterial stiffness variable were added to the models.

Lastly, we stratified the participants by quartiles of cfPWV, AIx and CPP and assessed the associations of increasing quartiles with "worsening of hypertension" during follow-up using multivariable logistic regression models adjusted in stepwise fashion as in the linear regression models above. "Worsening of hypertension" was defined as a difference between absolute BP values between the 2nd and 1st visits >0.

Statistical analyses were performed with SPSS vs. 21 (IBM Corp., Armonk, NY), and a *P* value ≤0.05 was considered to be statistically significant.

Results

The mean±SD age at the time of the first visit was 60±8 years, 55% were women, and 14% were diabetic. The average interval between the 2 study visits was 8.5±0.9 years. More participants were being treated with anti-hypertensives at the time of the 2nd visit (96%) than at the first visit (91%), and the average number of anti-hypertensives per participant increased over time (1.5±0.8 at the 1st visit, 2.1±1.0 at the 2nd visit, $P<0.0001$). Despite the increase in the number of hypertension drugs, average SBP, MAP and PP increased over time (Table 2).

Linear regression assumptions were tested and satisfied. Independent predictors of increases in SBP, DBP, MAP and PP over time are depicted in Table 3. These variables were included in the final multivariable models. The results of the multivariable linear regression models are outlined in Table 4. Baseline cfPWV was directly associated with changes in SBP and PP, and inversely associated with changes in DBP, but not associated with changes in MAP. Baseline AIx was directly associated with changes in SBP, DBP and MAP, but not with changes in PP. Baseline CPP was directly associated with changes in SBP, MAP and PP, but not with changes in DBP. When we calculated individual Z scores for each BP component during both visits, and repeated the analyses utilizing a difference in Z scores as the dependent variable rather than absolute BP difference, inferences remained unchanged (analyses not shown). When we repeated the models adjusting for anti-hypertensive drug classes (diuretics, beta blockers, calcium channel blockers and inhibitors of the renin-

angiotensin-aldosterone system) instead of difference in the number of anti-hypertensive drugs, the results remained unchanged (analyses not shown).

Interaction term analyses showed that age was a significant effect modifier of the associations of AIx and CPP with longitudinal changes in MAP. When we stratified the sample into age < and ≥65 years, we found that AIx and CPP were significantly associated with increases in MAP among those younger than 65 years (β±SE: 0.35±0.08 and 0.23±0.06, respectively, $P<0.0001$ for both) but not in those >65 years (β±SE: 0.04±0.10, $P=0.69$ and 0.18±0.09, P=0.052, respectively). We did not find significant associations between sex and arterial stiffness measures in the prediction of BP change over time.

The cutoff values for the 2nd, 3rd and 4th quartiles of cfPWV were 8.2 m/s, 9.4 m/s and 11.0 m/s, respectively; cutoff values for the 2nd, 3rd and 4th AIx quartiles were 27%, 33% and 39%, respectively; cutoff values for the 2nd, 3rd and 4th quartiles of CPP were 37 mmHg, 45 mmHg and 55 mmHg, respectively. Independent predictors of worsening of SBP, DBP, MAP and PP are listed in table 5. The results of the final multivariable logistic regression models are shown in Figure 1. Increasing quartiles of cfPWV were associated with worsening of SBP and PP; while increasing quartiles of AIx were associated with worsening of SBP and MAP, and increasing quartiles of CPP were associated with worsening of SBP, MAP and PP. As an example, a participant with a baseline cfPWV greater than 11 m/s was 2.5 times more likely to experience an increase in SBP and 3.6 times more likely to experience an increase in PP during follow-up than a participant whose cfPWV at baseline was lower than 8.2 m/s. Inferences were similar when worsening of hypertension was defined as a difference in BP value Z scores between the 2nd and 1st visits > 0 (analyses not shown).

Discussion

In a community-based cohort of hypertensive individuals, most of whom were receiving anti-hypertensive therapy (91% and 96% at the 1st and 2nd visits, respectively), we investigated the associations of measures of arterial stiffness with changes in BP over a mean period of 8.5 years, and found that arterial stiffness was associated with longitudinal increases in SBP, MAP and PP, and decrease in DBP. Our findings are relevant for clinical practice as they highlight arterial stiffness as a possible key factor in the pathophysiology of progression of hypertension, an important health burden(5) with associated high morbidity, mortality (1,2,5,6) and health care costs.(5) Notably, few of the clinical parameters were associated with hypertension progression, and baseline SBP and DBP were actually inversely associated with BP increases over time, which may have occurred due to regression towards the mean. Thus, our data show that relying solely on the clinical variables is imperfect when trying to predict the risk of hypertension progression. Non-invasive markers that identify hypertensive individuals at risk for worsening of their disease over time will be valuable for risk stratification and to individualize therapies that may help prevent the adverse consequences of hypertension. Based on our findings, measures of arterial stiffness, which can be relatively inexpensively and non-invasively obtained in the office, are candidate markers for such approach.

In addition, we found that the associations of AIx and CPP with MAP was only present in younger (< 65 years) subjects. Previous studies in the general population have shown that AIx increases with age until approximately age 60, when it then plateaus and then subsequently drops slightly, [25] due to predominant aortic stiffening and decrease in wave reflections with aging. As such, AIx/ wave reflections also have a greater contribution to CPP in younger than in older individuals. [25] In addition, while MAP increases with aging in those younger than age 55, the elderly predominantly experience longitudinal increases in PP with only little changes in MAP.[25] These changes in BP hemodynamics with aging likely explain the exclusive association of AIx and CPP with MAP in younger subjects.

Another interesting observation was that the association of brachial SBP with PP worsening was inverse, and that of DBP with PP worsening was direct, suggesting that baseline brachial PP was inversely associated with PP increase; while the baseline CPP was directly associated with PP increase. These findings are consistent with our finding that aortic stiffness is associated with hypertension progression, and can be explained on the basis of peripheral pulse pressure amplification: In younger and healthy subjects, there is greater amplification of pulse pressure from the aorta to peripheral arteries (Brachial PP/ central PP> 1.0). With aging and aortic stiffening, pressure amplification is reduced, with central PP approximating or even surpassing peripheral PP. As such, a greater CPP in respect to brachial PP denotes greater arterial stiffness, and based on the findings from our study, is a better predictor of PP worsening over time.

In normotensive individuals from the general population, measures of arterial stiffness are associated with increases in BP over time, and with incident hypertension. Liao et al(19) studied nearly 7000 normotensive individuals from the ARIC study and found that carotid stiffness predicted incidence of hypertension after 6 years of follow-up. In 1759 individuals from the Framingham Offspring Cohort,(13) 40% of whom were hypertensive, arterial stiffness (assessed by cfPWV, AIx and forward pressure wave amplitude) was associated with higher BP at follow-up, after a mean of 6.5 years. The association of these measures with longitudinal changes in BP was not assessed, however. In a cohort of 449 normotensive (n=306) and untreated hypertensive (n=143) individuals, Najjar et al (20) also found that cfPWV predicted increases in BP over time as well as incident hypertension. In addition, in 475 Japanese individuals with high-normal BP, (21) and in 2512 Greek normotensives, arterial stiffness (assessed by the brachial ankle pulse wave velocity in the former study, and by echocardiography in the latter) also predicted future development of hypertension. The converse association, however, is controversial. While AlGhatrif et al demonstrated that higher baseline BP was associated with faster increases in aPWV over time, (22) Kaess et al showed that baseline BP was not associated with higher aPWV after 7 years of follow-up. (13)

To the best of our knowledge, our study is the first to prospectively assess whether arterial stiffness is associated with longitudinal increases in BP in treated hypertensives. In multivariable models we found that there were few significant predictors of longitudinal BP changes and worsening of hypertension in treated hypertensives (baseline SBP, DBP and history of myocardial infarction, although eGFR and history of smoking also predicted changes in DBP, and the difference in the number of anti-hypertensives between the 2 visits

also predicted changes in MAP), limiting the ability to identify individuals at risk for hypertension progression based on clinical and laboratory characteristics alone, and underscoring the usefulness of arterial stiffness measures in this setting. Our findings support the use of arterial tonometry in hypertensives to identify those at greatest risk of hypertension progression and its related adverse outcomes.

In contrast to previous studies of hypertensives that showed that SBP and DBP decreased over time, (23–26) we found that BP measures increased in up to 80% (for increases in PP) of participants in our study. BP can be divided into a steady component, MAP, and a pulsatile component, PP. Although both MAP and PP increased on average, PP increased more so than MAP (+13±3 mmHg compared to + 3±1 mmHg in 8.5 years). This is consistent with previous studies in the general population,(13,27) and suggests that progressive stiffening of the aorta plays a major role in the increase in BP over time, since a compliant aorta is necessary to maintain a low PP for a given stroke volume. This further corroborates our findings and highlights arterial stiffness as a key determinant of the increases in BP in hypertensive individuals despite treatment.

We have previously shown that women have greater proximal aortic stiffness and peripheral wave reflection, and consequently, higher central pulse pressure than men.(28) However, in the present study, worsening of hypertension was not more common in women, and the associations of arterial stiffness measures with changes in BP over time did not differ based on sex. Thus, although arterial stiffness seems to differentially affect cardiac function and ventricular-arterial coupling in women, it is associated with future worsening of hypertension in both sexes. We did not measure proximal aortic stiffness (aortic characteristic impedance) at baseline, and in the context of our previous findings,(28) it is possible that an association of aortic characteristic impedance with worsening of hypertension may differ in men and women, which remains amenable for future studies.

Strengths and Limitations

The main strengths of our study are its community-based and prospective nature, the relatively long follow-up period, and the focus on treated hypertensives. A limitation is the restriction to non-Hispanic whites, and therefore further studies are necessary in hypertensive individuals of other ethnic groups. In addition, the cohort may not have been sufficiently powered to detect weaker predictors of BP change over time. Further, the BP recorded during the study visits may not accurately reflect BP oscillations during the day. However, our methods for assessing BP were standardized, performed in a controlled research setting, and similar to the methods used in previous studies of this topic. Lastly, we did not have data on long-term alcohol, caffeine and dairy consumption, and although we had comprehensive data on anti-hypertensive medication use, we cannot comment on changes in the doses of these medications over time.

Conclusions

In a community-based cohort of treated hypertensive individuals, measures of arterial stiffness (cfPWV, AIx and CPP) independently predicted longitudinal increases in BP. These results highlight measurement of arterial stiffness as a potential tool to identify

hypertensive individuals at greater risk for worsening of their hypertension and who may be candidates for more aggressive risk management strategies. Arterial tonometry is non-invasive, relatively inexpensive, and can be performed in the office setting. In addition, our findings motivate further studies of arterial stiffness as a therapeutic target to prevent worsening of hypertension, and ultimately, end-organ damage and cardiovascular events.

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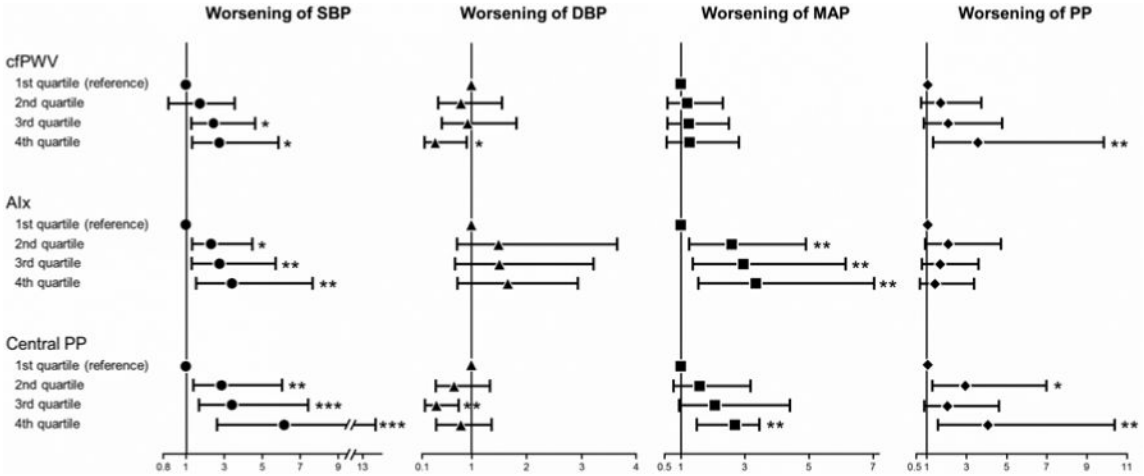

Figure 1. Associations of quartiles of arterial stiffness measures with worsening of hypertension

The figure depicts the point estimates of odds ratio and respective 95% confidence intervals for the associations of each baseline measure of arterial stiffness with 'worsening' of SBP, DBP, MAP and PP, which was defined as a difference in each BP value between 2nd and 1st visits >0.

*$P \leq 0.05$ **$P \leq 0.01$ ***$P \leq 0.001$

Table 1

Baseline characteristics of the participants at the time of the first visit

Variable (n=414)	Mean±SD or n (%)
Age, years	60±8
Women, n (%)	227 (55%)
Use of anti-hypertensive medications, n (%)	378 (91%)
Use of beta- blockers, n (%)	175 (42%)
Use of calcium channel blockers, n (%)	67 (16%)
Use of diuretics, n (%)	203 (49%)
Use of RAAS inhibitors, n (%)	187 (45%)
Use of statins, n (%)	154 (37%)
History of ever smoking, n (%)	196 (47%)
History of diabetes, n (%)	58 (14%)
History of myocardial infarction, n (%)	27 (7%)
History of stroke, n (%)	10 (2.1%)
Body mass index, kg/m^2	31.4±5.7
Waist circumference, cm	103.0±15.8
Serum creatinine, μmol/L *	79.6±21.2
Estimated glomerular filtration rate, (mL/s/1.73 m)†	1.1±0.2
cfPWV, m/s	9.7±2.6
AIx (%)	32.3±10.0
Central pulse pressure, mmHg	46±13

AIx: aortic augmentation index. cfPWV: carotid-femoral pulse wave velocity. RAAS: renin-angiotensin-aldosterone system.

* To convert serum creatinine to mg/dL, divide the value by 88.4.

† To convert estimated glomerular filtration rate to ml/min/1.73m^2, divide the value by 0.01667.

Table 2

Changes in blood pressure components between the 2 study visits

Variable (n=414)	First study (mean±SD)	Second study (mean±SD)	*P*-value
Brachial SBP (mmHg)	134±16	141±18	<0.0001
Brachial DBP (mmHg)	75±9	70±10	<0.0001
Brachial MAP (mmHg)	95±10	98±11	<0.0001
Brachial PP (mmHg)	58±14	71±17	<0.0001
Number of anti-hypertensive medications	1.5±0.8	2.1±1.0	<0.0001
Percent of participants whose blood pressure parameters increased over time			
Brachial SBP, n (%)	269 (65%)		
Brachial DBP, n (%)	112 (27%)		
Brachial MAP, n (%)	250 (62%)		
Brachial PP, n (%)	332 (80%)		

DBP: diastolic blood pressure. MAP: mean arterial pressure. PP: pulse pressure. SBP: systolic blood pressure.

Table 3

Independent predictors of increases in systolic, diastolic, mean and pulse pressure over time

	β ± SE	*P*-value
Predictors of SBP increase		
History of MI	10.61±3.24	0.001
Baseline SBP, mmHg	−0.59±0.06	<0.0001
Baseline DBP, mmHg	−0.23±0.12	0.05
Predictors of DBP increase		
History of smoking	1.78±0.83	0.03
History of MI	4.08±1.69	0.02
Baseline SBP, mmHg	−0.12±0.03	<0.0001
Baseline DBP, mmHg	−0.48±0.06	<0.0001
eGFR, mL/min/1.73 m^2	0.13±0.04	0.001
Predictors of MAP increase		
History of MI	5.86±2.05	0.004
Baseline SBP, mmHg	−0.22±0.04	<0.0001
Baseline DBP, mmHg	−0.42±0.08	<0.0001
Difference in the number of anti-hypertensives	−1.39±0.63	0.03
Predictors of PP increase		
History of MI	6.53±3.19	0.04
Baseline SBP, mmHg	−0.48±0.06	<0.0001
Baseline DBP, mmHg	0.25±0.10	0.02

Results of linear regression models using absolute blood pressure difference between 2^{nd} and 1^{st} visits as the dependent variable.

eGFR: estimated glomerular filtration rate. MI: myocardial infarction. Other abbreviations as in Table 2.

Table 4

Associations of arterial stiffness measures with changes in blood pressure components over time

Arterial stiffness measure	Δ blood pressure component	β±SE	*P* value
cfPWV (m/s)	SBP (mmHg)	0.71±0.31	0.02
	DBP (mmHg)	−0.37±0.18	0.04
	MAP (mmHg)	−0.03±0.23	0.91
	PP (mmHg)	1.09±0.27	<0.0001
AIx (%)	SBP (mmHg)	0.23±0.10	0.02
	DBP (mmHg)	0.16±0.04	<0.0001
	MAP (mmHg)	0.27±0.07	<0.0001
	PP (mmHg)	0.06±0.08	P0.47
CPP (mmHg)	SBP (mmHg)	0.44±0.07	P<.0001
	DBP (mmHg)	0.02±0.04	P0.60
	MAP (mmHg)	0.24±0.05	P<0.0001
	PP (mmHg)	0.42±0.06	P<0.0001

Linear regression models were adjusted for age, sex, time interval between studies, baseline SBP and DBP, history of diabetes, smoking, myocardial infarction and stroke, BMI, glomerular filtration rate, use of statins and difference in the number of anti-hypertensive medications between 2^{nd} and 1^{st} visits. We used a criteria of P<0.10 to enter, and P≤0.05 to stay in the models. Final covariates included in each model are shown in Table 3. AIx: aortic augmentation index. cfPWV: carotid-femoral pulse wave velocity. CPP: central pulse pressure. DBP: diastolic blood pressure. MAP: mean arterial pressure. PP: pulse pressure. SBP: systolic blood pressure. SE: standard error

Table 5

Independent predictors of SBP, DBP, MAP and PP worsening over time

	OR (95% CI)	*P*-value
Predictors of SBP worsening		
History of MI	2.58 (1.00, 6.79)	0.05
History of diabetes	2.47 (1.18, 5.18)	0.02
Statin use	0.59 (0.34, 1.00)	0.05
Baseline SBP, 1 mmHg	0.93 (0.91, 0.95)	<0.0001
Predictors of DBP worsening		
Baseline SBP, 1 mmHg	0.97 (0.95, 0.99)	0.02
Baseline DBP, 1 mmHg	0.90 (0.87, 0.94)	<0.0001
Predictors of MAP worsening		
Female sex	1.90 (1.10, 3.30)	0.02
History of smoking	2.04 (1.25, 3.33)	0.004
Baseline SBP, 1 mmHg	0.96 (0.94, 0.97)	<0.0001
Baseline DBP, 1 mmHg	0.95 (0.92, 0.98)	0.001
eGFR, 1 mL/min/1.73 m^2	1.03 (1.01, 1.05)	0.001
Predictors of PP worsening		
Age, 1 year	1.04 (1.01, 1.08)	0.02
Baseline SBP, 1 mmHg	0.93 (0.91, 0.95)	<0.0001
Baseline DBP, 1 mmHg	1.04 (1.01, 1.08)	0.02

"Worsening" was defined as a difference between blood pressure measures between the 2^{nd} and 1^{st} visits >0. AIx: aortic augmentation index. cfPWV: carotid-femoral pulse wave velocity. CI: confidence interval. CPP: central pulse pressure. DBP: diastolic blood pressure. MAP: mean arterial pressure. OR: odds ratio. PP: pulse pressure. SBP: systolic blood pressure. SE: standard error