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Research Article

Arterial stiffness is associated with increase in blood pressure over time in treated hypertensives

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Abstract

Arterial stiffness is associated with incident hypertension. We hypothesized that measures of arterial stiffness would predict increases in systolic (SBP), mean (MAP), and pulse pressure (PP) over time in treated hypertensives. 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 three 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. SBP, MAP, and PP increased in 80% of participants. After adjustment for covariates listed, cfPWV (m/s) was associated with increases in SBP (β ± standard error [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 (mmHg) 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 ($P \leq .02$ for each). In conclusion, arterial stiffness measures were associated with longitudinal increases in SBP, MAP, and PP in treated hypertensives. J Am Soc Hypertens 2014;8(6):414–421.

Keywords: Hypertension; pulse wave velocity; pulse pressure; augmentation index.

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 one in three 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 is 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 end-organs. As the aorta stiffens, there are greater swings in BP, pulse pressure increases, cardiac function is impaired,

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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 BP is more likely to increase over time. 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 [cfPWV], aortic augmentation index [AIx], and central pulse pressure [CPP]) 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 two separate occasions (between January 2003 and December 2008, and between October 2009 and December 2011). The GENOA study is community-based study to identify genetic variants influencing BP levels and the development of target-organ damage due to hypertension. Participants belong to sibships with at least two 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 three 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 $\geq$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 three measures of arterial stiffness: cfPWV, considered the gold standard measure of aortic stiffness, AIx, a measure of arterial wave reflection, and CPP, a global measure of arterial stiffness. Participants were asked to fast for 12 hours and withhold vasoactive medications, alcohol, and caffeine 24 hours 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] Distances from the carotid sampling site to the manubrium sternum and from the manubrium sternum to the femoral artery were measured by tape. 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 $\pm$ standard deviation (SD). Differences in BP parameters between the first and second 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 second visit – BP at first 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