Hemodynamic Correlates of Blood Pressure in Older Adults: The Atherosclerosis Risk in Communities (ARIC) Study

Hirofumi Tanaka, PhD;[1] Gerardo Heiss, MD;[2] Elizabeth L. McCabe, PhD;[3] Michelle L. Meyer, PhD;[2] Amil M. Shah, MD;[3] Judy R. Mangion, PhD;[3] Justina Wu, MD;[3] Scott D. Solomon, MD;[3] Susan Cheng, MD[3]

From the University of Texas at Austin, Austin, TX;[1] University of North Carolina at Chapel Hill, Chapel Hill, NC;[2] and Brigham and Women's Hospital, Harvard Medical School, Boston, MA[3]

The primary aim of the present study was to identify the hemodynamic correlates of both steady and pulsatile blood pressure (BP) in community-dwelling older adults. In 3762 adults aged 70 to 89 years, significant hemodynamic determinants of both brachial and carotid systolic BP included arterial stiffness as measured by aortic pulse wave velocity, stroke volume (via echocardiography), arterial wave reflection, left ventricular ejection time, and upstroke time. The strongest influence was exerted by arterial stiffness. The steady-state component of blood pressure, mean arterial pressure, was associated with both cardiac index and total peripheral resistance (TPR), but was more strongly associated with TPR. Results were similar when participants taking antihypertensive medications were excluded from analyses. The overall findings suggest that mean arterial pressure is associated strongly with TPR and that significant hemodynamic correlates of systolic BP included arterial stiffness, stroke volume, and arterial wave reflection. *J Clin Hypertens (Greenwich).* 2016;18:1222–1227.

Arterial pressure increases progressively with advancing age, resulting in a high prevalence of essential hypertension. This rise in blood pressure (BP) with age is a major contributor to age-related increases in numerous cardiovascular disorders.[1] While systolic BP (SBP) rises continuously, diastolic BP plateaus and tends to decline after 50 to 60 years of age.[2] Accordingly, pulse pressure increases markedly with advancing age, resulting in a high prevalence of isolated systolic hypertension.[3]

Although the trend of age-associated increases in BP is well established, it remains unclear what hemodynamic factors determine BP levels in older adults. Arterial BP can be divided into both steady-state and pulsatile components. The steady-state component of BP is represented by mean arterial pressure and is a critically important cardiovascular measure from the physiological standpoint, as it is the effective pressure that determines perfusion to the vital organs. Mean arterial pressure is determined exclusively by cardiac output and total peripheral resistance as governed by Ohm's law. The hemodynamic factors that influence the pulsatile component, on the other hand, are much more complex. SBP is governed by a number of hemodynamic factors, including arterial stiffness, stroke volume, and left ventricular ejection fraction, whereas the primary hemodynamic determinants of diastolic pressure include total peripheral resistance, heart rate, arterial stiffness, and SBP. The relative contribution of each hemodynamic factor is currently unknown, especially in older adults, as most of the available evidence is derived from circulatory modeling studies or comparisons with a single hemodynamic variable.[4–6]

We evaluated a comprehensive number of hemodynamic determinants of BP in Atherosclerosis Risk in Communities (ARIC) study cohort. The availability of comprehensive tonometric measures in ARIC provided an added opportunity to separately interrogate correlates of both peripheral and central BP. The latter approach is clinically important in light of increasing evidence that central, compared with peripheral, BP may be more predictive of cardiovascular and other morbid outcomes.[7] Accordingly, the primary aim of the present study was to characterize the hemodynamic determinants of steady-state and pulsatile BP in community-dwelling older adult participants in the ARIC study.

METHODS

Patients

The ARIC study is an ongoing, population-based longitudinal study involving four US communities (Forsyth County, NC; Jackson, MS; Minneapolis, MN; and Washington County, MD). A total of 6533 participants (65% response rate from 10,036 eligible participants) attended ARIC study visit 5 (in years 2011–2013) and underwent a standardized examination.[8] For the present analyses, we excluded participants with missing information on BP, arterial stiffness, and/or echocardiography, body mass index $\geq$40 kg/m^2, major arrhythmias (Minnesota codes

Address for Correspondence: Hirofumi Tanaka, PhD, Department of Kinesiology and Health Education, University of Texas at Austin, 2109 San Jacinto Boulevard, D3700, Austin, TX 78712
E-mail: htanaka@austin.utexas.edu

Manuscript received: March 31, 2016; **revised:** May 26, 2016; **accepted:** June 9, 2016
DOI: 10.1111/jch.12898

8-1-3, 8-3-1, and 8-3-2: ≥10% atrial, and ventricular premature beats, atrial fibrillation, or flutter), peripheral vascular disease (aortic aneurysms, abdominal aorta ≥5 cm, history of aortic or peripheral revascularization or presence of an aortic graft, or aortic stenosis), other major cardiovascular disease (history of coronary artery disease, heart failure, or stroke), and moderate or greater aortic regurgitation. Participants who self-identified as Asian and African American from Minnesota and Maryland field centers were excluded because of small numbers. After exclusions, the final analytic sample included 3762 participants. Institutional review boards approved the study protocol at each field center and participating institution, and all study participants provided written informed consent.

Measurements

Participants were asked not to consume food or drinks and to refrain from tobacco and vigorous physical activity after midnight prior to the visit or for 8 hours prior to the visit. Participants were also asked to bring all prescription and nonprescription medications taken within 2 weeks. Blood samples were obtained following a standardized venipuncture protocol and were assayed in ARIC central laboratories. Diabetes was defined as fasting glucose ≥126 mg/dL, nonfasting glucose ≥200 mg/dL, antidiabetic medication use, or self-reported diagnosis of diabetes.

Brachial BP (systolic, mean, and diastolic BP) was measured twice with the participants in the supine position using oscillometric automated sphygmomanometer (VP-1000 Plus, Omron Healthcare, Kyoto, Japan), and the average measurement was used for analyses. Stroke volume and cardiac output were calculated based on two-dimensional echocardiographic measurements (IE33, Philips Healthcare, Andover, MA) performed with excellent reproducibility in our core laboratory, as previously described.[9] Echocardiographic measures were indexed to body surface area, where appropriate. Total peripheral resistance was calculated as mean arterial pressure divided by the cardiac index. Carotid-femoral pulse wave velocity, an index of arterial stiffness, and carotid artery pressure waveforms were obtained using an automatic vascular screening device (VP-1000 Plus, Omron Healthcare) as previously described[10] with excellent reproducibility.[11] Carotid and femoral arterial pressure waveforms were acquired for 30 seconds by applanation tonometry sensors attached on the left common carotid artery (via neck collar) and left femoral artery (via elastic tape around the hip). Augmentation index (AIx), an index of arterial wave reflection, carotid systolic pressure, ejection time, and upstroke time were obtained from the carotid pressure waveform analyses.[5] AIx measured by this machine is strongly associated with that obtained with SphygmoCor (AtCor Medical, West Ryde, Australia).[12] Vascular and cardiac measurements were performed on different days.

Statistical analyses

All statistical analyses were conducted using SAS version 9.4 (SAS Institute Inc, Cary, NC). Associations between BP and hemodynamic variables were evaluated using multivariable linear regression and partial correlational analyses. Adjusted models included age, sex, race, body mass index, and current smoking status. Separate analyses were performed in the total sample of 3762 participants and in the subgroup of 1204 participants not taking antihypertensive medications at the time of the examination. A two-sided $P<.05$ was considered statistically significant.

RESULTS

The average SBP was 137±17 mm Hg and a majority of participants (68%) were taking antihypertensive medications at the time of the examination (Table I).

Table II displays multivariable-adjusted associations of both brachial and carotid SBP measures with hemodynamic variables. All the hemodynamic variables examined were significantly associated with both brachial and carotid SBP except for ejection fraction.

TABLE I. Characteristics of the Study Participants

Characteristic	Total Sample (N=3762)
Age, y	75±5
Women, %	63
Black, %	21
Body mass index, kg/m^2	28±4
Obesity, %	30
Diabetes, %	23
Total cholesterol, mmol/L	4.9±1.0
LDL cholesterol, mmol/L	2.8±0.9
HDL cholesterol, mmol/L	1.4±0.4
Triglycerides, mmol/L	1.4±0.7
eGFR, mL/min	71.7±16.1
Antihypertensive medication, %	68
Current smoker, %	5
Heart rate, beats per min	65±10
Systolic BP, mm Hg	137±17
Diastolic BP, mm Hg	73±9
Mean BP, mm Hg	100±13
Carotid systolic BP, mm Hg	144±22
Carotid AIx, %	19.5±16.0
cfPWV, cm/s	1146±295
SV index, mL/m^2	28.1±6.0
CO index, mL/min/m^2	1801±391
TPR, U	0.03±0.01
LVEF, %	66±10
Reduced LVEF <30%, %	0.05

Abbreviations: AIx, augmentation index; BP, blood pressure; cfPWV, carotid-femoral pulse wave velocity; CO, cardiac output; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; LVEF, left ventricular ejection fraction; SV, stroke volume; TPR, total peripheral resistance.

Values are shown as mean±standard deviation or percent frequency.

TABLE II. Multivariable-Adjusted Hemodynamic Correlates of Brachial and Carotid Systolic Pressures

Hemodynamic Parameter	Total Sample (N=3762)			Nonmedicated (n=1204)		
	Coefficient (SE)	Partial R^2	*P* Value	Coefficient (SE)	Partial R^2	*P* Value
Brachial systolic pressure						
cfPWV	0.02 (0.0009)	0.134	<.0001	0.02 (0.002)	0.121	<.0001
SV index	1.71 (0.30)	0.009	<.0001	1.80 (0.50)	0.011	.0004
AIx	4.50 (0.29)	0.067	<.0001	4.17 (0.49)	0.060	<.0001
LVEF	−0.05 (0.29)	0.000009	.86	−0.66 (0.49)	0.002	.18
ET	3.37 (0.28)	0.040	<.0001	2.35 (0.51)	0.017	<.0001
UT	−2.15 (0.28)	0.016	<.0001	−2.25 (0.50)	0.017	<.0001
Carotid systolic pressure						
cfPWV	0.02 (0.001)	0.089	<.0001	0.02 (0.002)	0.091	<.0001
SV index	2.97 (0.38)	0.016	<.0001	2.65 (0.63)	0.014	<.0001
AIx	4.83 (0.37)	0.045	<.0001	4.22 (0.62)	0.039	<.0001
LVEF	0.70 (0.36)	0.001	.05	0.11 (0.61)	0.00003	.86
ET	5.94 (0.34)	0.072	<.0001	4.53 (0.63)	0.040	<.0001
UT	−2.35 (0.36)	0.011	<.0001	−2.54 (0.62)	0.014	<.0001

Abbreviations: AIx, augmentation index; cfPWV, carotid-femoral pulse wave velocity; ET, ejection time; LVEF, left ventricular ejection fraction; SE, standard error; SV, stroke volume; UT, upstroke time.

All analyses were adjusted for age, sex, black race, body mass index, diabetes, and current smoking status. Coefficients represent change in systolic pressure per 1-standard deviation change in the hemodynamic parameter.

For both brachial and carotid systolic pressure, the hemodynamic variables that contributed the most variation to systolic pressure (as represented by the partial R^2 value) were arterial stiffness followed by AIx and ejection time. The results were similar when the analyses were repeated after excluding the participants taking antihypertensive medications.

In an attempt to determine whether the associations between BP and hemodynamic parameters are affected by age, the study cohort was divided according to the age categories that approximate tertiles (<75, 75 to <80, and ≥80 years) (Table III). The strength of associations between arterial stiffness and SBP became weaker with increasing age while associations with stroke volume and AIx became stronger.

When analyses were repeated using pulse pressure, the overall results were similar to those observed for SBP (Table IV). Ejection time was the most prominent hemodynamic determinant of variation in both brachial and systolic pulse pressure in the total study sample, followed by arterial stiffness. Stroke volume, in addition to AIx, was also among the hemodynamic measures that was observed to contribute significant variation to measures of pulse pressure. When the participants were divided into age tertiles, contribution of ejection time to pulse pressure became greater with increasing age (Table V).

The multivariable-adjusted hemodynamic correlates of mean BP are shown in Table VI. We observed relatively small contributions of cardiac index and TPR to variation in mean BP in regression models that adjusted for all the clinical covariates. Mean BP was associated with both cardiac index and total peripheral resistance; however, total peripheral resistance was the primary hemodynamic determinant of variation in mean BP. The results were similar when the participants who had been taking antihypertensive medications were excluded from these analyses.

DISCUSSION

Arterial BP progressively increases with advancing age, resulting in a high prevalence of essential hypertension in the population at large. Indeed, in our community-based study sample of predominantly older adults, the prevalence of hypertension was over 70%. As implied by the term *essential* hypertension, the physiological factors that contribute to the steady rise in BP in aging adults remain largely unknown. Thus, in the present study, we interrogated the distinct steady-state and pulsatile components of BP and examined the hemodynamic correlates of these components measured both peripherally and centrally.

The steady-state component of BP is characterized by mean arterial BP and is determined by cardiac output and peripheral resistance via the Ohm's law. Of these two factors, total peripheral resistance displayed the more dominant influence on mean arterial pressure in the present sample of community-dwelling older adults. These results are consistent with previous small-scale cross-sectional studies showing that the elevation in mean arterial pressure with aging is related to an increase in total peripheral resistance because cardiac output typically declines.[5,6] The steady-state BP component based on Ohm's law is useful in gaining physiological insight. However, it may not be appropriate to apply to an aging population because mean arterial pressure does not increase much with adult aging attributable to age-related declines in diastolic BP

TABLE III. Multivariable-Adjusted Hemodynamic Correlates of Brachial and Carotid Systolic Pressures in the Total Sample (N=3762), by Age Group

	Age <75 y			Age 75–<80 y			Age ≥80 y		
Parameter	Coefficient (SE)	Partial R^2	*P* Value	Coefficient (SE)	Partial R^2	*P* Value	Coeffient (SE)	Partial R^2	*P* Value
Brachial SBP									
cfPWV	0.03 (0.001)	0.158	<.0001	0.02 (0.002)	0.123	<.0001	0.02 (0.002)	0.094	<.0001
SV index	1.32 (0.40)	0.006	.0009	2.04 (0.57)	0.013	.0004	2.55 (0.69)	0.020	.002
AIx	3.82 (0.38)	0.051	<.0001	4.73 (0.55)	0.074	<.0001	5.93 (0.70)	0.101	<.0001
LVEF	−0.95 (0.40)	0.003	.02	0.99 (0.52)	0.004	.06	0.69 (0.63)	0.002	.27
ET	2.94 (0.38)	0.029	<.0001	3.25 (0.52)	0.038	<.0001	4.48 (0.59)	0.075	<.0001
UT	−1.62 (0.39)	0.009	<.0001	−2.11 (0.53)	0.016	<.0001	−3.35 (0.63)	0.039	<.0001
Carotid SBP									
cfPWV	0.03 (0.002)	0.106	<.0001	0.02 (0.002)	0.080	<.0001	0.02 (0.002)	0.071	<.0001
SV index	2.42 (0.51)	0.011	<.0001	3.21 (0.72)	0.019	<.0001	4.25 (0.81)	0.036	<.0001
AIx	4.03 (0.49)	0.033	<.0001	5.07 (0.72)	0.049	<.0001	6.35 (0.85)	0.073	<.0001
LVEF	−0.63 (0.52)	0.0007	.22	2.19 (0.66)	0.011	.0009	1.75 (0.75)	0.007	.02
ET	5.57 (0.48)	0.060	<.0001	5.79 (0.66)	0.069	<.0001	6.72 (0.70)	0.108	<.0001
UT	−1.63 (0.50)	0.005	.001	−2.56 (0.67)	0.014	.0002	−3.53 (0.77)	0.028	<.0001

Abbreviations: AIx, augmentation index; cfPWV, carotid-femoral pulse wave velocity; ET, ejection time; LVEF, left ventricular ejection fraction; SBP, systolic blood pressure; SV, stroke volume; UT, upstroke time.

All analyses were adjusted for age, sex, black race, body mass index, and current smoking status. Coefficients represent change in systolic pressure per 1-standard deviation change in the hemodynamic parameter.

TABLE IV. Multivariable-Adjusted Hemodynamic Correlates of Brachial and Carotid Pulse Pressures

Hemodynamic	Total Sample (N=3762)			Nonmedicated (n=1204)		
Parameter	Coefficient (SE)	Partial R^2	*P* Value	Coefficient (SE)	Partial R^2	*P* Value
Brachial pulse pressure						
cfPWV	0.01 (0.0006)	0.083	<.0001	0.01 (0.001)	0.069	<.0001
SV index	2.22 (0.20)	0.030	<.0001	1.90 (0.34)	0.024	<.0001
AIx	2.14 (0.20)	0.030	<.0001	1.90 (0.33)	0.026	<.0001
LVEF	0.74 (0.20)	0.004	.0002	0.04 (0.33)	0.00001	.90
ET	4.03 (0.18)	0.112	<.0001	3.11 (0.33)	0.063	<.0001
UT	−1.31 (0.19)	0.011	<.0001	−1.29 (0.34)	0.011	.0001
Carotid pulse pressure						
cfPWV	0.01 (0.001)	0.042	<.0001	0.014 (0.002)	0.045	<.0001
SV index	3.51 (0.31)	0.032	<.0001	2.73 (0.49)	0.023	<.0001
AIx	2.42 (0.31)	0.016	<.0001	2.03 (0.48)	0.014	<.0001
LVEF	1.38 (0.30)	0.005	<.0001	0.45 (0.48)	0.0007	.36
ET	6.51 (0.27)	0.122	<.0001	5.20 (0.48)	0.082	<.0001
UT	−1.46 (0.30)	0.006	<.0001	−1.30 (0.49)	0.005	.008

Abbreviations: AIx, augmentation index; cfPWV, carotid-femoral pulse wave velocity; ET, ejection time; LVEF, left ventricular ejection fraction; SV, stroke volume; UT, upstroke time.

All analyses were adjusted for age, sex, black race, body mass index, diabetes, and current smoking status. Coefficients represent change in pulse pressure per 1-standard deviation change in the hemodynamic parameter.

that offset corresponding increases in SBP. Furthermore, in clinical practice, hypertension is typically defined in terms of systolic and diastolic BP, and mean BP is usually not even calculated.

In the present study, we included a variety of hemodynamic measures that have been described as physiological correlates of SBP, and we examined the associations between potential hemodynamic determinants and noninvasively measured SBP. We observed that most of the hemodynamic determinants, including arterial stiffness, stroke volume, arterial wave reflection, left ventricular ejection time, and upstroke time, were significantly related to brachial systolic pressure. The only hemodynamic measure that did not display significant associations with SBP was left ventricular ejection fraction, possibly due to attrition-related sampling bias (ie, ARIC study participants who died prior to visit 5 were more likely to have had reduced ejection fraction).

TABLE V. Multivariable-Adjusted Hemodynamic Correlates of Brachial and Carotid Pulse Pressures in the Total Sample (N=3762), by Age Group

	Age <75 y			Age 75–<80 y			Age ≥80 y		
Parameter	Coefficient (SE)	Partial R^2	*P* Value	Coefficient (SE)	Partial R^2	*P* Value	Coefficient (SE)	Partial R^2	*P* Value
Brachial PP									
cfPWV	0.01 (0.0009)	0.100	<.0001	0.01 (0.001)	0.077	<.0001	0.01 (0.001)	0.072	<.0001
SV index	1.78 (0.27)	0.020	<.0001	2.62 (0.38)	0.044	<.0001	3.03 (0.48)	0.051	<.0001
AIx	1.59 (0.26)	0.018	<.0001	2.50 (0.38)	0.043	<.0001	2.88 (0.52)	0.044	<.0001
LVEF	0.21 (0.28)	0.0003	.44	1.43 (0.35)	0.016	<.0001	1.24 (0.45)	0.010	.006
ET	3.66 (0.25)	0.093	<.0001	3.72 (0.034)	0.104	<.0001	5.06 (0.40)	0.178	<.0001
UT	−0.84 (0.26)	0.005	.002	−1.68 (0.36)	0.021	<.0001	−2.03 (0.46)	0.026	<.0001
Carotid PP									
cfPWV	0.02 (0.001)	0.055	<.0001	0.01 (0.002)	0.033	<.0001	0.01 (0.002)	0.041	<.0001
SV index	2.88 (0.42)	0.22	<.0001	3.94 (0.59)	0.040	<.0001	4.73 (0.69)	0.057	<.0001
AIx	1.80 (0.40)	0.010	<.0001	2.66 (0.60)	0.019	<.0001	3.34 (0.75)	0.027	<.0001
LVEF	0.47 (0.43)	0.0005	.28	2.60 (0.54)	0.021	<.0001	2.04 (0.65)	0.013	.002
ET	6.16 (0.38)	0.107	<.0001	6.18 (0.52)	0.113	<.0001	7.26 (0.57)	0.169	<.0001
UT	−0.77 (0.41)	0.002	.06	−2.21 (0.56)	0.014	<.0001	−2.14 (0.65)	0.014	.001

Abbreviations: AIx, augmentation index; cfPWV, carotid-femoral pulse wave velocity; ET, ejection time; LVEF, left ventricular ejection fraction; PP, pulse pressure; SV, stroke volume; UT, upstroke time.

All analyses were adjusted for age, sex, black race, body mass index, and current smoking status. Coefficients represent change in pulse pressure per 1-standard deviation change in the hemodynamic parameter.

TABLE VI. Multivariable-Adjusted Hemodynamic Correlates of Mean Blood Pressure Based on Ohm's Law

Hemodynamic	Total Sample (N=3762)			Nonmedicated (n=1204)		
Parameter	Coefficient (SE)	Partial R^2	*P* Value	Coefficient (SE)	Partial R^2	*P* Value
Cardiac index	0.74 (0.21)	0.003	.0005	1.11 (0.38)	0.007	.003
TPR	6.29 (0.21)	0.151	<.0001	6.29 (0.39)	0.178	<.0001

Abbreviations: SE, standard error; TPR, total peripheral resistance.

All analyses were adjusted for age, sex, black race, body mass index, and current smoking status. Coefficients represent change in mean blood pressure per 1-standard deviation change in the hemodynamic parameter.

An increase in the stiffness of the large elastic arteries located in the cardiothoracic (central) circulation (eg, aorta and carotid artery) has been implicated as the primary mechanism underlying the age-associated increase in SBP and pulse pressure.[13,14] Indeed, the strongest relation with SBP was observed with arterial stiffness as measured by pulse wave velocity. The increase in central artery stiffness observed with adult aging likely occurs because of changes in both functional and structural determinants within the vascular wall.[13,15] However, age-related increases in arterial stiffness do not appear to be dependent on the presence of clinical atherosclerotic disease. The stiffening of arteries with advancing age has been observed in a rural Chinese population in whom the prevalence of atherosclerosis is very low[16,17] and in rigorously screened US men and women,[18–20] as well as in beagle dogs who are resistant to atherosclerosis.[21] Interestingly, when the study cohort was divided into approximate tertiles, the strength of associations between arterial stiffness and SBP became weaker with increasing age while associations with stroke volume and AIx became stronger. These results suggest that the role of arterial stiffness as a primary determinant of pulsatile BP component may get diminished with advancing age.

To date, studies of the hemodynamic determinants of BP have largely focused on peripheral (ie, brachial) BP. Thus, the determinants of central BP have been inferred but not established. One of the strengths of the present analyses is the inclusion of central (ie, carotid) BP assessment. Central BP is more directly related than peripheral BP to cardiac afterload and coronary perfusion during diastole.[7] Accordingly, central BP is considered a more accurate and robust cardiovascular prognostic marker than conventional brachial BP and is differentially affected by antihypertensive medications.[22,23] We observed that hemodynamic correlates of central systolic pressure included arterial stiffness, stroke volume, arterial wave reflection, left ventricular ejection time, and upstroke time. The strengths of these associations were fairly similar to those observed for peripheral (ie, brachial) BP.

STUDY STRENGTHS AND WEAKNESSES

The strengths of the present study include its very large sample size involving older adults as well as comprehensive measures of hemodynamic factors. However, there are also a number of limitations that should be emphasized. First, the cross-sectional nature of the present analyses cannot provide any information regarding causality or longitudinal changes. Second, a major confounding factor for the present analyses was the high prevalence of antihypertensive medication use. Therefore, we performed separate analyses in the subset of individuals not taking antihypertensive medications and observed very similar results to those from the analyses of the total sample. However, it should be noted that there are a number of coexisting conditions that we could not account for fully with statistical analyses. Conversely, we were not able to address the effects of certain antihypertensive medications. Third, the present sample was primarily composed of older adults; thus, the extent to which our results can be extended to younger populations is unknown. Finally, the strengths of associations between BP and hemodynamic factors were modest, likely due in large part to the fact that all measurements were performed noninvasively at a single point in time in this large epidemiologic cohort. As such, our results should be interpreted with caution.

CONCLUSIONS

The findings of the present study in community-dwelling older adults indicate that mean arterial pressure is strongly associated with cardiac output and particularly with systemic vascular resistance. Significant hemodynamic determinants of SBP included arterial stiffness, stroke volume, arterial wave reflection, left ventricular ejection time, and upstroke time with the strongest influence exerted by arterial stiffness. We also showed that these factors similarly impacted central BP. Understanding physiological factors that determine components of BP should lead to better prevention and treatment strategies for the epidemics of hypertension.

Acknowledgments: The ARIC study is carried out as a collaborative study supported by National Heart, Lung, and Blood Institute contracts (HHSN268201100005C, HHSN268201100006C, HHSN268201100007C, HHSN268201100008C, HHSN268201100009C, HHSN268201100010C, HHSN268201100011C, and HHSN268201100012C). This work was also supported by NIGMS grant T32 GM74905 (ELM), NHLBI cooperative agreement NHLBI-HC-11-08 (SDS), grants R00-HL-107642 (SC) and K08-HL-116792 (AMS), a grant from the Ellison Foundation (SC), and grant 14CRP20380422 from the American Heart Association (AMS).

Conflict of Interest: None.

References

1. Lee ML, Rosner BA, Weiss ST. Relationship of blood pressure to cardiovascular death: the effects of pulse pressure in the elderly. *Ann Epidemiol*. 1999;9:101–107.
2. Kannel WB, Gordon T. Evaluation of cardiovascular risk in the elderly: the Framingham study. *Bull NY Acad Med*. 1978;54:573–591.
3. Benetos A, Safar M, Rudnichi A, et al. Pulse pressure: a predictor of long-term cardiovascular mortality in a French male population. *Hypertension*. 1997;30:1410–1415.
4. Messerli FH, Frohlich ED, Suarez DH, et al. Borderline hypertension: relationship between age, hemodynamics and circulating catecholamines. *Circulation*. 1981;64:760–764.
5. Tanaka H, Dinenno FA, Hunt BE, et al. Hemodynamic sequelae of age-related increases in arterial stiffness in healthy humans. *Am J Cardiol*. 1998;82:1152–1155.
6. Hunt BE, Davy KP, Jones PP, et al. Systemic hemodynamic determinants of blood pressure in women: age, physical activity, and hormone replacement. *Am J Physiol*. 1997;273:H777–H785.
7. Agabiti-Rosei E, Mancia G, O'Rourke MF, et al. Central blood pressure measurements and antihypertensive therapy: a consensus document. *Hypertension*. 2007;50:154–160.
8. Meyer ML, Tanaka H, Palta P, et al. Correlates of segmental pulse wave velocity in older adults: the Atherosclerosis Risk in Communities (ARIC) Study. *Am J Hypertens*. 2016;29:114–122.
9. Shah AM, Cheng S, Skali H, et al. Rationale and design of a multicenter echocardiographic study to assess the relationship between cardiac structure and function and heart failure risk in a biracial cohort of community-dwelling elderly persons: the Atherosclerosis Risk in Communities study. *Circ Cardiovasc Imaging*. 2014;7:173–181.
10. Tanaka H, Munakata M, Kawano Y, et al. Comparison between carotid-femoral and brachial-ankle pulse wave velocity as measures of arterial stiffness. *J Hypertens*. 2009;27:2022–2027.
11. Meyer ML, Tanaka H, Palta P, et al. Repeatability of central and peripheral pulse wave velocity measures: the Atherosclerosis Risk in Communities (ARIC) study. *Am J Hypertens*. 2016;29:470–475.
12. Dhindsa M, Barnes JN, Devan AE, et al. Comparison of augmentation index derived from multiple devices. *Artery Res*. 2011;5:112–114.
13. O'Rourke MF. Arterial aging: pathophysiological principles. *Vasc Med*. 2007;12:329–341.
14. Arnett DK, Boland LL, Evans GW, et al. Hypertension and arterial stiffness: the Atherosclerosis Risk in Communities Study. *Am J Hypertens*. 2000;13:317–323.
15. Mitchell GF, Parise H, Benjamin EJ, et al. Changes in arterial stiffness and wave reflection with advancing age in healthy men and women: the Framingham Heart Study. *Hypertension*. 2004;43:1239–1245.
16. Avolio AP, Fa-Quan D, Wei-Qiang L, et al. Effects of aging on arterial distensibility in populations with high and low prevalence of hypertension: comparison between urban and rural communities in China. *Circulation*. 1985;71:202–210.
17. Avolio AP, Chen SG, Wang RP, et al. Effects of aging on changing arterial compliance and left ventricular load in a northern Chinese urban community. *Circulation*. 1983;68:50–58.
18. Vaitkevicious PV, Fleg JL, Engel JH, et al. Effects of age and aerobic capacity on arterial stiffness in healthy adults. *Circulation*. 1993;88:1456–1462.
19. Tanaka H, DeSouza CA, Seals DR. Absence of age-related increase in central arterial stiffness in physically active women. *Arterioscler Thromb Vasc Biol*. 1998;18:127–132.
20. Tanaka H, Dinenno FA, Monahan KD, et al. Aging, habitual exercise, and dynamic arterial compliance. *Circulation*. 2000;102:1270–1275.
21. Haidet GC, Wennberg PW, Finkelstein SM, Morgan DJ. Effects of aging per se on arterial stiffness: systemic and regional compliance in beagles. *Am Heart J*. 1996;132:319–327.
22. Williams B, Lacy PS, Thom SM, et al. Differential impact of blood pressure-lowering drugs on central aortic pressure and clinical outcomes: principal results of the Conduit Artery Function Evaluation (CAFE) study. *Circulation*. 2006;113:1213–1225.
23. de Luca N, Mallion JM, O'Rourke MF, et al. Regression of left ventricular mass in hypertensive patients treated with perindopril/indapamide as a first-line combination: the REASON echocardiography study. *Am J Hypertens*. 2004;17:660–667.