Received: 16 March 2022 | Revised: 21 April 2022 | Accepted: 23 April 2022

DOI: 10.1111/jch.14493

ORIGINAL ARTICLE

WILEY

Arterial stiffness and contralateral differences in blood pressure: The Atherosclerosis Risk in Communities (ARIC) study

Daniela Charry MSH[1] | Natalia Gouskova PhD[2] | Michelle L. Meyer PhD[3] | Kimberley Ring MPH[3] | Vijay Nambi MD[4] | Gerardo Heiss PhD[4] | Hirofumi Tanaka PhD[1]

[1]Department of Kinesiology and Health Education, The University of Texas at Austin, Austin, Texas, USA

[2]Hinda and Arthur Marcus Institute for Aging Research, Hebrew SeniorLife, Harvard Medical School, Boston, Massachusetts, USA

[3]Department of Epidemiology, Gillings School of Global Public Health, University of North Carolina, Chapel Hill, North Carolina, USA

[4]Department of Cardiology, Baylor College of Medicine, Houston, Texas, USA

Correspondence
Hirofumi Tanaka, PhD, Department of Kinesiology and Health Education, The University of Texas at Austin, 2109 San Jacinto Blvd, D3700, Austin, TX 78712, USA.
Email: htanaka@austin.utexas.edu

Abstract

A large interarm difference in brachial systolic blood pressure (SBP) (≥10 or ≥15 mmHg) is strongly associated with elevated cardiovascular events and mortality. Evidence demonstrating whether such contralateral differences in SBP occur in ankle blood pressure and its association with arterial stiffness is scarce. The aims of this study were to characterize arm and ankle contralateral SBP differences in a sample of community-dwelling older adults (5077), and to determine whether this difference is associated with arterial stiffness assessed by pulse wave velocity (PWV) between the heart and ankle (haPWV), femoral artery and ankle (faPWV), and brachial artery and ankle (baPWV) in the right and left sides. Prevalence of interarm SBP differences ≥10 and ≥15 mmHg was 5.1% and .7%, respectively; the corresponding prevalence for interankle SBP was 24.9% and 12.0%. Higher BMI and lower ankle-brachial index (ABI) were significantly correlated with greater interarm SBP differences. Increased age, higher BMI, lower ABI, and greater contralateral differences in haPWV, faPWV, and baPWV were significantly correlated to greater interankle SBP differences. Interankle SBP difference ≥15 mmHg was significantly associated with contralateral differences of >80 cm/s in haPWV (OR = 1.94 [95% CI = 1.52–2.49]), >165 cm/s in faPWV (OR = 1.64 [95% CI = 1.27–2.12]), and >240 cm/s in baPWV (OR = 2.43 [95% CI = 1.94–3.05]). The associations remained significant after adjustment for age, sex, race, BMI, smoking status, and ABI. Compared with interarm differences, interankle differences in SBP are common in older adults. The magnitude of interankle, but not interarm, differences in SBP is associated with various measures of arterial stiffness.

KEYWORDS
aging, arterial stiffness, inter-arm difference, pulse wave velocity

1 | INTRODUCTION

Blood pressure is a prototypical quantitative trait known to be variable. It fluctuates beat-by-beat from daytime to nighttime. Blood pressure can be substantially different in each limb that is measured.[1–4] Several epidemiological studies have demonstrated that a large interarm difference in brachial systolic blood pressure (SBP) (i.e., ≥10 or ≥15 mmHg) is associated with elevated cardiovascular events and mortality.[2–6] Pathophysiology linking contralateral differences in brachial SBP and cardiovascular mortality remains unclear, but subclinical and/or clinical vascular disease affecting one side of the body (e.g., coarctation, subclavian artery stenosis) has been suggested.[3,4,7] Physiological factors such as arterial stiffness could also play a role as SBP is strongly influenced by the stiffening of arteries.[8,9] Indeed, individual variabilities in contralateral differences in pulse wave velocity (PWV) have been reported,[10] but there is of yet published no information addressing this question. Moreover, it is not known if such contralateral differences in ankle SBP are associated with those in brachial blood pressure. Considering the evidence that arterial wave reflection is a primary mechanism responsible for augmenting SBP distally, and that the lower body is believed to be the important site of wave reflection,[11] contralateral differences in SBP, if any, may be influenced by the stiffness of arteries to a greater extent in the ankle than in the arm. However, such issue has not been addressed. The Atherosclerosis Risk in Communities (ARIC) study utilized a vascular screening device that simultaneously measured blood pressure in four limbs and arterial stiffness in both sides of the body,[12] which enables a comprehensive examination of blood pressure differences and their associations with arterial stiffness.

Accordingly, the aims of the present study were to characterize arm and ankle contralateral SBP differences in a sample of community-dwelling older adults and to determine whether these differences are associated with various measures of arterial stiffness assessed at different body sites.

2 | METHODS

2.1 | Study population

The ARIC Study is a community-based prospective cohort study of atherosclerosis. In total, 15,792 black and white adults, aged 45–64 years at baseline, were recruited from four US communities: Jackson, Mississippi; Forsyth County, North Carolina; suburbs of Minneapolis, Minnesota; and Washington County, Maryland. Participants completed subsequent clinic examinations and the fifth one (visit 5, 2011–2013) included the assessment of PWV.

In total, 6538 participants attended visit 5. Exclusions included non-white and nonblack participants, body mass index (BMI) ≥40 kg/m^2, major arrhythmias (Minnesota code 8-1-3, 8-3-1, and 8-3-2), aortic aneurysms, history of aortic or peripheral revascularization or aortic graft, aortic stenosis, moderate or greater aortic regurgitation, and missing covariates of interest. Our final sample included 5077 participants with available PWV and simultaneous assessment of SBP in the four limbs. The study was approved by the Institutional Review Boards at all centers, and all participants gave informed consent.

2.2 | Pulse wave velocity

The semiautomatic vascular screening device OMRON VP-1000 plus (Kyoto, Japan) was used to measure blood pressure simultaneously in the arms and ankles and arterial stiffness by PWV after participants were in the supine position for 5–10 min. Participant preparation included abstaining from smoking, vigorous exercise, and caffeinated beverages during the day of examination. PWV was estimated as the distance between 2 arterial recording sites divided by transit time. PWV was assessed between the heart and ankle (haPWV), femoral artery and ankle (faPWV), and brachial artery and ankle (baPWV) on the right and left sides. Femoral arterial pressure waveforms were acquired for 30 s by applanation tonometry sensor attached to the left common femoral artery (via elastic tape around the hip). Bilateral brachial and posterior-tibial arterial pressure waveforms were detected over 10 s by extremity cuffs connected to a plethysmographic and an oscillometric pressure sensor wrapped on both arms and ankles. Trained technicians recorded PWV and blood pressures twice, and the results of the two readings were averaged.[8]

2.3 | Covariates

Participants underwent a blood draw, standard 12-lead electrocardiogram, anthropometric measurements, and interviewer-administered questionnaires to obtain medical history and lifestyle information. Age, sex, race, smoking status, and medical history were self-reported. The smoking status classified participants as never smokers, former smokers, or current smokers. Body weight was measured to the nearest .1 kg, and height was recorded to the nearest centimeter. BMI was calculated as body weight (kg)/height (m^2). Ankle-brachial index (ABI), the ratio of ankle SBP to brachial SBP was calculated for right and left legs using the higher value of the right or left brachial SBP as the denominator (OMRON VP-1000 plus). Blood samples were obtained via venipuncture, and enzymatic assays for high-density lipoprotein (HDL) cholesterol, triglycerides, and glucose were performed. Low-density lipoprotein (LDL) cholesterol was calculated using the Friedewald equation. Hypertension was defined as SBP ≥140 mmHg, diastolic blood pressure ≥90 mmHg, or antihypertensive medication use as they were the diagnostic criteria at the time of the testing. Diabetes was defined as fasting glucose concentration of ≥126 mg/dl, nonfasting glucose of ≥200 mg/dl, glucose lowering medication use, or self-reported diagnosis of diabetes.

2.4 | Statistical analyses

Data were analyzed using SAS 9.4 (SAS Institute, Cary, NC). Variables are presented as means ± SD if continuous and as count (percent) if categorical. Analysis was performed after excluding potential outliers,

defined as PWV and SBP values 3 SDs above or below the mean. Baseline characteristics were compared between individuals with and without interarm and interankle SBP difference ≥10 mmHg and ≥15 mmHg using *t*-tests.[13,14] Pearson correlations and multivariable logistic regression were used to examine relations between characteristics associated with contralateral differences in arm and in ankle SBP. Odds ratio (OR) and 95% confidence intervals (CI) were calculated to determine the association between contralateral differences in arm and ankle SBP ≥10 and ≥15 mmHg and contralateral differences in haPWV > 80 cm/s, faPWV > 165 cm/s, and baPWV > 240 cm/s. The cut points for contralateral differences in PWV were arbitrarily set at the 90th percentile in our sample. We also performed the analysis using the 75th and 50th percentile (data not shown). Two models were created, Model 1 was unadjusted, and Model 2 was adjusted for age, sex, race, BMI, smoking status, and ABI. The level of significance was set at $p < .05$ for all tests. Additionally, using a stepwise backward elimination process, covariates that did not contribute significantly were removed and excluded from the final analysis. These are presented as parsimonious models to elucidate the relationship between the variables. Furthermore, sensitivity analysis was performed to exclude the possibility that the accuracy of PWV readings might be affected by ABI < .95 ($n = 4656$).

3 | RESULTS

Of the 5077 adults studied, 41% were male, 21.5% blacks, with a mean age of 75.2 ± 5.1 years. Overall sample characteristics stratified by interarm and interankle SBP differences of ≥10 mmHg and ≥15 mmHg are shown in Table 1. The mean ± SD absolute contralateral differences in arm and ankle SBP were 3.7 ± 3.0 and 7.5 ± 7.0 mmHg, respectively. The prevalence of interarm SBP differences of ≥10 and ≥15 mmHg were 5.1 and .7%, and the corresponding prevalence for interankle SBPs were 24.9% and 12.0%. Pearson correlation analysis showed a moderate relationship between right brachial and right ankle SBP ($r = .66$, $p < .0001$) and between left brachial and left ankle SBP ($r = .67$, $p < .0001$). However, there was no significant correlation between interarm and interankle differences in SBP. Higher BMI and lower ABI were significantly correlated with greater interarm SBP differences ($r = .16$ and $r = -.14$, $p < .0001$, respectively). Increased age ($r = .08$), higher BMI ($r = .08$), lower ABI ($r = -.22$), and greater contralateral differences in haPWV ($r = .13$), faPWV ($r = .09$), and baPWV ($r = .15$) were significantly correlated to greater interankle SBP differences ($p < .0001$).

As compared with participants with interankle SBP differences of <10 mmHg and <15 mmHg, those with differences of ≥10 mmHg and ≥15 mmHg were more likely to have worse cardiovascular risk factor profiles, such as a higher prevalence of current smoking, hypertension, and diabetes ($p < .05$) (Table 1). They also had higher brachial SBP, lower ABI, and higher triglycerides ($p < .05$). The prevalence of ABI < .95 was also greater (15.3% and 24.1% vs. 5.9% and 6.1%, $p < .05$, respectively).

Similarly, those with interarm differences of ≥10 mmHg and ≥15 mmHg had a higher prevalence of current smoking and hypertension ($p < .05$). In addition, they had higher BMI, brachial SBP, lower ABI, and higher triglycerides (only in those with a difference of ≥15 mmHg) ($p < .05$). When comparing subjects who demonstrated both interankle SBP difference and interarm SBP differences ≥10 mmHg or ≥15 mmHg to those with either one alone, we did not find significant differences in cardiovascular risk profiles.

Interankle SBP difference of ≥10 mmHg was significantly associated with contralateral differences of >80 cm/s in haPWV (OR = 1.49 [95% CI = 1.21–1.83]), > 165 cm/s in faPWV (OR = 1.31 [95% CI = 1.06–1.61]), and >240 cm/s in baPWV (OR = 1.76 [95% CI = 1.45–2.13]). Only the association with baPWV remained statistically significant after adjustment for age, sex, race, BMI, smoking status, and ABI. Parsimonious models for haPWV and baPWV were adjusted for age, sex, BMI, and ABI. For faPWV, sex, race, BMI, and ABI were included (Table 2).

Interankle SBP difference of ≥15 mmHg was significantly associated with contralateral differences of >80 cm/s in haPWV (OR = 1.94 [95% CI = 1.52–2.49]), >165 cm/s in faPWV (OR = 1.64 [95% CI = 1.27–2.12]), and >240 cm/s in baPWV (OR = 2.43 [95% CI = 1.94–3.05]). The associations remained statistically significant after adjustment for covariates. Parsimonious models for haPWV and baPWV were adjusted for age, sex, race, BMI, and ABI. For faPWV the significant variables were the same except for age, which did not significantly contribute to the model (Table 2).

The results from the sensitivity analysis in subjects with ABI > .95 were attenuated but remained statistically significant. Interankle SBP difference of ≥10 mmHg was associated with contralateral differences in haPWV (OR = 1.27 [95% CI = 1.00–1.62]), and in baPWV (OR = 1.49 [95% CI = 1.19–1.87]). Interankle SBP difference of ≥15 mmHg was related to contralateral differences in haPWV (OR = 1.53 [95% CI = 1.12–2.10]), faPWV (OR = 1.55 [95% CI = 1.13–2.12]), and baPWV (OR = 2.01 [95% CI = 1.52–2.67]) (Table 3).

In this sample, neither interarm SBP difference of ≥10 mmHg nor ≥15 mmHg were significantly associated with contralateral differences of >80 cm/s in haPWV, >165 cm/s in faPWV, and >240 cm/s in baPWV (Tables 4 and 5). Similar results were obtained using the 75th and 50th percentile.

When examining interankle SBP differences as a continuous variable, every 1-standard deviation (7 mmHg) increase in interankle SBP differences resulted in a 15%, 14%, and 28% increased odds of having a contralateral difference in haPWV > 80 cm/s, faPWV > 165 cm/s, and baPWV > 240 cm/s, respectively ($p < .001$). When examining interarm SBP differences as a continuous variable, none of the associations were statistically significant ($p = .5$, $p = .2$, and $p = .5$ respectively).

4 | DISCUSSION

In this population-based study using a simultaneous measurement of blood pressure and arterial stiffness, we evaluated the association between contralateral SBP differences and arterial stiffness by PWV. We found that the prevalence of interankle differences in SBP of ≥10 mmHg and ≥15 mmHg were common, namely 25 and 12%. Our

TABLE 1 Comparison of selected subject characteristics stratified by interankle and interarm differences in systolic blood pressure (SBP)

		Inter-ankle SBP difference		Inter-arm SBP difference		Inter-ankle SBP difference		Inter-arm SBP difference	
	Overall	<10 mmHg	≥10 mmHg	<10 mmHg	≥10 mmHg	<15 mmHg	≥15 mmHg	<15 mmHg	≥15 mmHg
Participants, *n*	5077 (100)	3809 (75.1)	1268 (24.9)	4815 (94.9)	262 (5.1)	4,472 (88.0)	605 (12.0)	5,042 (99.3)	35 (.7)
Age, year	75.2 ± 5.17	75.1 ± 5.13	75.8 ± 5.26	75.3 ± 5.17	75.0 ± 5.16	75.1 ± 5.12	76.3 ± 5.40	75.2 ± 5.17	75.2 ± 5.18
Sex, *n* (%)									
Male	2098 (41.3)	1516 (39.8)	582 (45.9)	2006 (41.7)	92 (35.1)	1804 (40.4)	294 (48.6)	2087 (41.4)	11 (31.4)
Female	2979 (58.7)	2293 (60.2)	686 (54.1)	2809 (58.3)	170 (64.9)	2668 (59.6)	311 (51.4)	2955 (58.6)	24 (68.6)
Race, *n* (%)									
Black	1089 (21.5)	759 (19.9)	330 (26.0)	1010 (21.0)	79 (30.2)	907 (20.3)	182 (30.1)	1076 (21.3)	13 (37.1)
White	3988 (78.5)	3050 (80.1)	938 (74.0)	3805 (79.0)	183 (69.8)	3565 (79.7)	423 (69.9)	3966 (78.7)	22 (62.9)
Smoking, *n* (%)									
Never smoked	2734 (53.9)	2029 (53.3)	705 (55.6)	2606 (54.1)	128 (48.9)	2384 (53.3)	350 (57.9)	2717 (53.9)	17 (48.6)
Former smoker	2048 (40.3)	1571 (41.2)	477 (37.6)	1934 (40.2)	114 (43.5)	1839 (41.1)	209 (34.5)	2034 (40.3)	14 (40.0)
Current smoker	295 (5.8)	209 (5.5)	86 (6.8)	275 (5.7)	20 (7.6)	249 (5.6)	46 (7.6)	291 (5.8)	4 (11.4)
Height (cm)	166 ± 9	165 ± 9	166 ± 9	166 ± 9	165 ± 9	166 ± 9	166 ± 10	166 ± 9	165 ± 11
BMI (kg/m^2)	27.9 ± 4.5	27.8 ± 4.5	28.5 ± 4.6	27.9 ± 4.5	29.9 ± 4.7	27.8 ± 4.5	28.6 ± 4.7	27.9 ± 4.5	30.9 ± 5.9
Brachial SBP (mmHg)	137 ± 17	136 ± 17	139 ± 3	137 ± 17	139 ± 21	137 ± 17	140 ± 18	137 ± 18	144 ± 22
Ankle SBP (mmHg)	157 ± 25	158 ± 23	155 ± 29	157 ± 25	159 ± 30	158 ± 24	153 ± 31	158 ± 25	158 ± 24
Ankle-brachial index	1.13 ± .1	1.14 ± .1	1.10 ± 01	1.13 ± .1	1.08 ± .1	1.13 ± .1	1.07 ± .1	1.13 ± .1	1.04 ± .1
Fasting glucose (mmol/l)	6.2 ± 1.4	6.2 ± 1.4	6.3 ± 1.5	6.2 ± 1.5	6.5 ± 1.6	6.2 ± 1.4	6.3 ± 1.7	6.2 ± 1.5	6.6 ± 1.8
LDL cholesterol (mmol/l)	2.72 ± .8	2.72 ± .8	2.70 ± .9	2.72 ± .8	2.65 ± .8	2.73 ± .8	2.64 ± .9	2.72 ± .8	2.52 ± .7
HDL cholesterol (mmol/l)	1.36 ± .3	1.37 ± .3	1.33 ± .3	1.36 ± .3	1.34 ± .3	1.36 ± .3	1.31 ± .3	1.36 ± .3	1.26 ± .2
Triglycerides (mmol/l)	1.41 ± .7	1.41 ± .7	1.42 ± .7	1.41 ± .7	1.46 ± .7	1.41 ± .7	1.46 ± .7	1.41 ± .7	1.76 ± .9
Hypertension, *n* (%)	3655 (71.9)	2679 (70.3)	976 (76.9)	3453 (71.7)	202 (77.1)	3168 (70.8)	487 (80.4)	3629 (71.9)	26 (74.2)
Diabetes, *n* (%)	1521 (29.9)	1078 (28.3)	443 (34.9)	1425 (29.5)	96 (36.6)	1283 (28.6)	238 (39.3)	1506 (29.8)	15 (42.9)

Note: Data are means ± SD or *n* (percentages).
Abbreviations: BMI, body mass index; LDL, low-density lipoprotein; HDL, high-density lipoprotein.

TABLE 2 Association between contralateral differences in ankle systolic blood pressure ≥10 mmHg and ≥15 mmHg and arterial stiffness as assessed by pulse wave velocity (PWV)

	≥10 mmHg		≥15 mmHg	
	OR	95% CI	OR	95% CI
haPWV > 80 cm/s				
Model 1	1.49***	1.21–1.83	1.94***	1.52–2.49
Model 2	1.21	.97–1.52	1.40**	1.06–1.84
Parsimonious model	1.23*	.99–1.53	1.44**	1.10–1.90
faPWV > 165 cm/s				
Model 1	1.31**	1.06–1.61	1.64**	1.27–2.12
Model 2	1.14	.91–1.44	1.32**	1.00–1.75
Parsimonious model	1.12	.90–1.39	1.33**	1.00–1.75
baPWV > 240 cm/s				
Model 1	1.76***	1.45–2.13	2.43***	1.94–3.05
Model 2	1.43**	1.15–1.78	1.79***	1.38–2.33
Parsimonious model	1.48**	1.19–1.84	1.88**	1.45–2.43

Note: Model 1: unadjusted; Model 2: adjusted for age, sex, race, BMI, smoking status, and ABI; Parsimonious models: haPWV and baPWV (≥10 mmHg): age, sex, BMI, and ABI; haPWV and baPWV (≥15 mmHg): age, sex, race, BMI, and ABI; faPWV (both): sex, race, BMI, and ABI; ***$p < .0001$; **$p < .05$; *$p = .06$.

TABLE 3 Association between contralateral differences in ankle systolic blood pressure ≥10 mmHg and ≥15 mmHg and arterial stiffness as assessed by pulse wave velocity (PWV) in subjects with ABI > .95

	≥10 mmHg		≥15 mmHg	
	OR	95% CI	OR	95% CI
haPWV > 80 cm/s				
Model 1	1.27**	1.00–1.62	1.53**	1.12–2.10
Model 2	1.17	.97–1.51	1.47**	1.06–2.04
Parsimonious Model	1.18	.97–1.52	1.48**	1.07–2.06
faPWV > 165 cm/s				
Model 1	1.18	.92–1.50	1.55**	1.13–2.12
Model 2	1.10	.86–.42	1.63**	1.18–2.25
Parsimonious Model	1.12	.87–1.45	1.52**	1.11–2.09
baPWV > 240 cm/s				
Model 1	1.49**	1.19–1.87	2.01***	1.52–2.67
Model 2	1.35**	1.05–1.73	1.81**	1.33–2.48
Parsimonious model	1.38**	1.07–1.76	1.82**	1.33–2.48

Note: Model 1: unadjusted; Model 2: adjusted for age, sex, race, BMI, smoking status, and ABI; Parsimonious models: haPWV and baPWV (≥10 mmHg): age, sex, BMI, and ABI; haPWV and baPWV (≥15 mmHg): age, sex, race, BMI, and ABI; faPWV (both): sex, race, BMI, and ABI; ***$p < .0001$; **$p < .05$.

findings showed that higher BMI, and lower ABI were significantly correlated to greater interarm SBP differences, while increased age, higher BMI, lower ABI, and greater contralateral differences in haPWV, faPWV, and baPWV were significantly correlated to greater interankle SBP differences. Those participants with interankle SBP difference of ≥15 mmHg were more likely to have contralateral differences of >80 cm/s in haPWV, >165 cm/s in faPWV, and >240 cm/s in baPWV. These associations remained significant even after adjustment for age, sex, race, BMI, smoking status, and ABI. When examining interankle SBP differences as a continuous variable, every 1-standard deviation (7 mmHg) increase in interankle SBP differences was associated with a 15%, 14%, and 28% increased odds of having a contralateral difference in haPWV > 80 cm/s, faPWV > 165 cm/s, and baPWV > 240 cm/s. Therefore, our data indicate that the magnitude of interankle, but not interarm, differences in SBP is associated with various measures of arterial stiffness in community-dwelling older adults.

Previous studies indicated SBP differences between arms carry prognostic information and that patients should have evaluation of blood pressure in both arms.[3] In addition, the ankle has been suggested as an alternative and/or additional site for noninvasive blood pressure measurement.[15,16] In the present study, blood pressure was measured simultaneously, bilaterally at both limbs using a validated oscillometric device.[12] Compared with sequentially repeated measurements of blood pressure with a single-cuff that is typically conducted, the simultaneous measurement may be more precise as beat-by-beat differences in blood pressure can be accounted for and can improve diagnostic accuracy.[14,18] Although brachial SBP was significantly associated with ankle SBP, interarm differences in SBP were not related to interankle differences in SBP suggesting that these contralateral differences in blood pressures may be modulated by different factors. Indeed, arterial stiffness was associated with interankle, but not with interarm, differences in SBP in the present study.

What are the explanations for the contribution of arterial stiffness to interankle SBP difference but a lack thereof to interarm differences? Arterial stiffening is a principal determinant of SBP[8] and has been independently associated with stroke, coronary disease severity, and cardiovascular outcome.[19] As the arterial wall stiffens, arterial wave reflection is a primary mechanism responsible for augmenting SBP.[8,9] In the arterial tree, branching points (i.e., aortic bifurcation, branches of renal arteries), areas of alteration in arterial elastance (from elastic artery to muscular artery), and high-resistance arterioles can all give rise to wave reflection and the lower body is believed to be an important site of wave reflection.[11] This cumulation of reflected waves along with the longer distance of the arterial tree to the ankle versus the upper arm is the reason that SBP at the level of the ankles is elevated in comparison to pressures measured in the arms in healthy humans.[20] It appears plausible that contralateral differences in SBP may be influenced to a greater extent by the stiffness of arteries in the ankle.

In the present study involving community-dwelling older adults, the prevalence of interarm SBP differences of ≥10 mmHg was 5.1%. A previous study from India reported a prevalence of 5% despite including participants with a wider age range (19–81 years).[6] The association between interarm differences in SBP and arterial stiffness has been evaluated in the past but remains highly controversial. For example, a systematic review and meta-analysis reported no association between

TABLE 4 Association between contralateral differences in brachial systolic blood pressure ≥10 mmHg and ≥15 mmHg and arterial stiffness as assessed by pulse wave velocity (PWV)

	≥10 mmHg		≥15 mmHg	
	OR	95% CI	OR	95% CI
haPWV > 80 cm/s				
Model 1	.90	.58–1.41	2.07	.85–5.01
Model 2	.83	.51–1.35	1.25	.41–3.79
Parsimonious model	.79	.49–1.29	1.70	.62–4.67
faPWV > 165 cm/s				
Model 1	1.04	.68–1.59	1.65	.64–4.28
Model 2	1.01	.64–1.60	1.71	.63–4.63
Parsimonious model	.95	.61–1.47	1.70	.62–4.67
baPWV > 240 cm/s				
Model 1	.84	.54–1.31	1.49	.57–3.85
Model 2	.76	.46–1.26	1.65	.59–4.57
Parsimonious model	.74	.45–1.22	1.70	.62–4.67

Note: Model 1: unadjusted; Model 2: adjusted for age, sex, race, BMI, smoking status, and ABI; Parsimonious model: haPWV and baPWV (both): age, sex, BMI, and ABI; faPWV (both): sex, race, BMI, and ABI. None of the associations were significant.

TABLE 5 Association between contralateral differences in brachial systolic blood pressure ≥10 mmHg and ≥15 mmHg and arterial stiffness as assessed by pulse wave velocity (PWV) in subjects with ABI > .95

	≥10 mmHg		≥15 mmHg	
	OR	95% CI	OR	95% CI
haPWV > 80 cm/s				
Model 1	1.03	.63–1.69	1.49	.45–4.99
Model 2	.97	.57–1.63	.93	.21–4.01
Parsimonious model	.91	.54–1.54	.91	.21–3.92
faPWV > 165 cm/s				
Model 1	1.08	.67–1.76	1.48	.44–4.93
Model 2	1.07	.65–1.76	1.44	.42–4.92
Parsimonious model	1.05	.64–1.72	1.43	.42–4.85
baPWV > 240 cm/s				
Model 1	.93	.56–1.52	1.35	.40–4.50
Model 2	.94	.56–1.59	1.62	.47–5.55
Parsimonious model	.93	.55–1.57	1.56	.46–5.32

Note: Model 1: unadjusted; Model 2: adjusted for age, sex, race, BMI, smoking status, and ABI; Parsimonious model: haPWV and baPWV (both): age, sex, BMI, and ABI; faPWV (both): sex, race, BMI, and ABI. None of the associations were significant.

interarm SBP difference of >10 mmHg and carotid-femoral PWV, but a positive association with baPWV.[21] Other studies[22,23] have reported a positive association between interarm differences in SBP ≥10 mmHg and PWV. Another study[18] also reported a relationship between interarm differences in SBP of ≥5 mmHg and arterial stiffness. However, this relationship was only found in patients with hypertension, and arterial stiffness was measured with a surrogate measure of pulse pressure/stroke volume index.[18] These conflicting findings could be a result of a smaller sample size, participants cardiovascular profile, a single measure of arterial stiffness, and the use of sequential BP measurements. In the present study, these experimental weaknesses are minimized or eliminated.

The prevalence of interankle SBP difference of >15 mmHg was 12.0% in the present study. This is consistent with a similar prevalence of interankle SBP difference of 13.7% observed in an older patient population referred for echocardiographic examinations in Taiwan.[1] Interankle differences in SBP ≥15 mmHg have been associated with arterial stiffness measured by baPWV.[1,20,23] High baPWV was independently associated with an interankle difference in SBP ≥15 mmHg or diastolic BP ≥10 mmHg. In addition, this difference was an independent predictor for overall mortality and cardiovascular mortality.[24] Our present results are consistent with these previous studies but provide unique insight into this issue as these data were obtained in a large community-based population of older adults using several measures of arterial stiffness (haPWV, faPWV, baPWV), and compared bilateral differences in PWV.

While higher absolute values of PWV indicate arterial stiffness, differences in PWV between the two sides of the body might also reflect a structural mismatch at reflecting sites of the arterial tree, especially in those with arterial stenosis. In cases of severe atherosclerosis, the stenosis of the arteries can affect PWV measurements. At the site of arterial stenosis, changes in the waveform can delay the derived PWV and affect contralateral differences in PWV.[25] In the present study, however, sensitivity analysis showed that associations between contralateral SBP differences and PWV remained statistically significant even after excluding participants with ABI < .95.

This study is not without limitations. First, results from our population of community-dwelling older adults may not be generalizable to other populations. Second, height-based formulas to calculate baPWV and faPWV were derived and validated in a Japanese population. Third, because of the cross-sectional nature of the study, the assessment of causality could not be confirmed. Future prospective studies are needed to address this issue.

In conclusion, the present study demonstrated that interankle SBP differences of ≥10 and ≥15 mmHg are common in older adults and that the magnitude of interankle, but not interarm differences in SBP is associated with several measures of arterial stiffness in community-dwelling older adults. These results expand the existing literature on factors that influence contralateral differences in blood pressure and open the opportunity for more optimum cardiovascular risk assessment. Future studies should evaluate whether contralateral differences in PWV could be regarded as an independent marker of arterial stiffness.

ACKNOWLEDGMENTS

The Atherosclerosis Risk in Communities 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). The arterial stiffness component of the study was supported by R01 AG053938.

CONFLICT OF INTEREST

None

AUTHOR CONTRIBUTIONS

Daniela Charry, Natalia Gouskova, Michelle L. Meyer, Vijay Nambi, Gerardo Heiss, and Hirofumi Tanaka designed and conceptualized the study. Daniela Charry, Natalia Gouskova, and Hirofumi Tanaka analyzed and interpreted the data. Daniela Charry and Hirofumi Tanaka drafted the manuscript for intellectual content. Natalia Gouskova, Michelle L. Meyer, Kimberley Ring, Vijay Nambi, Gerardo Heiss, and Hirofumi Tanaka revised the manuscript for intellectual content. All authors gave approval for submission of the final manuscript.

ORCID

Hirofumi Tanaka PhD https://orcid.org/0000-0002-1780-7471

REFERENCES

1. Su HM, Lin TH, Hsu PC, et al. Association of interankle systolic blood pressure difference with peripheral vascular disease and left ventricular mass index. *Am J Hypertens*. 2014;27(1):32-37.
2. Clark CE, Taylor RS, Shore AC, Ukoumunne OC, Campbell JL. Association of a difference in systolic blood pressure between arms with vascular disease and mortality: a systematic review and meta-analysis. *Lancet*. 2012;379(9819):905-914.
3. Agarwal R, Bunaye Z, Bekele DM. Prognostic significance of between-arm blood pressure differences. *Hypertension*. 2008;51(3):657-662.
4. Clark CE, Taylor RS, Butcher I, et al. Inter-arm blood pressure difference and mortality: a cohort study in an asymptomatic primary care population at elevated cardiovascular risk. *Br J Gen Pract*. 2016;66(646):e297-e308.
5. Jegatheswaran J, Hiremath S, Edwards C, Ruzicka M. Inter-arm difference in blood pressure in patients referred to tertiary hypertension center: prevalence, risk factors, and relevance to physicians. *J Clin Hypertens*. 2020;22(8):1513-1517.
6. Sharma B, Ramawat P. Prevalence of inter-arm blood pressure difference among clinical out-patients. *Int J Health Sci*. 2016;10(2):229-237.
7. Mansia G, De Backer G, Dominiczak A, et al. 2007 ESH-ESC guidelines for the management of arterial hypertension: the task force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *J Hypertens*. 2007;25(6):1105-1587.
8. Tanaka H, Heiss G, McCabe EL, et al. Hemodynamic correlates of blood pressure in older adults: the Atherosclerosis Risk in Communities (ARIC) study. *J Clin Hypertens*. 2016;18(12):1222-1227.
9. Berry KL, Cameron JD, Dart AM, et al. Large-artery stiffness contributes to the greater prevalence of systolic hypertension in elderly women. *J Am Geriatr Soc*. 2004;52(3):368-373.
10. Jago JR, Murray A. Repeatability of peripheral pulse measurements on ears, fingers and toes using photoelectric plethysmography. *Clin Phys Physiol Meas*. 1988;9(4):319-330.
11. Tarumi T, Sugawara J, Tanaka H. Association between ankle blood pressure and central arterial wave reflection. *J Hum Hypertens*. 2011;25(9):539-544.
12. Cortez-Cooper MY, Supak JA, Tanaka H. A new device for automatic measurements of arterial stiffness and ankle-brachial index. *Am J Cardiol*. 2003;91(12):1519-1522.
13. Weinberg I, Gona P, O'Donnell CJ, Jaff MR, Murabito JM. The systolic blood pressure difference between arms and cardiovascular disease in the Framingham Heart study. *Am J Med*. 2014;127(3):209-215.
14. Song X, Li G, Qiao A, Chen Z. Association of simultaneously measured four-limb blood pressures with cardiovascular function: a cross-sectional study. *Biomed Eng Online*. 2016;15(2):147.
15. Moore C, Dobson A, Kinagi M, Dillon B. Comparison of blood pressure measured at the arm, ankle and calf. *Anaesthesia*. 2008;63(12):1327-1331.
16. Hietanen H, Pääkkönen R, Salomaa V. Ankle and exercise blood pressures as predictors of coronary morbidity and mortality in a prospective follow-up study. *J Hum Hypertens*. 2010;24(9):577-584.
17. Sheppard JP, Albasri A, Franssen M, et al. Defining the relationship between arm and leg blood pressure readings: a systematic review and meta-analysis. *J Hypertens*. 2019;37(4):660-670.
18. Lida M, Ishiguro Y, Ueda N, Honjo H. Inter-arm difference of systolic blood pressure measured by automated double-cuff device is associated with arterial stiffness in patients with hypertension. *Blood Press Monit*. 2020;25(1):26-33.
19. Mattace-Raso FU, van der Cammen TJ, Hofman A, et al. Arterial stiffness and risk of coronary heart disease and stroke: the Rotterdam study. *Circulation*. 2006;113(5):657-663.
20. Aboyans V, Criqui MH, Abraham P, et al. Measurement and interpretation of the ankle-brachial index: a scientific statement from the American Heart Association. *Circulation*. 2012;126(24):2890-2909.
21. Singh S, Sethi A, Singh M, Khosla K, Grewal N, Khosla S. Simultaneously measured inter-arm and inter-ankle systolic blood pressure differences and cardiovascular risk stratification: a systemic review and meta-analysis. *J Am Soc Hypertens*. 2015;9(8):640-650.
22. Su HM, Lin TH, Hsu PC, et al. Association of interarm systolic blood pressure difference with atherosclerosis and left ventricular hypertrophy. *PLoS ONE*. 2012;7(8):e41173.
23. Canepa M, Milaneschi Y, Ameri P, et al. Relationship between inter-arm difference in systolic blood pressure and arterial stiffness in community-dwelling older adults. *J Clin Hypertens*. 2013;15(12):880-887.
24. Chen SC, Chang JM, Tsai YC, et al. Association of interleg BP difference with overall and cardiovascular mortality in hemodialysis. *Clin J Am Soc Nephrol*. 2012;7(10):1646-1653.
25. Motobe K, Tomiyama H, Koji Y, et al. Cut-off value of the ankle-brachial pressure index at which the accuracy of brachial-ankle pulse wave velocity measurement is diminished. *Circ J*. 2005;69(1):55-60.

How to cite this article: Charry D, Gouskova N, Meyer ML, et al. Arterial Stiffness And Contralateral Differences In Blood Pressure: the Atherosclerosis Risk In Communities (ARIC) Study. *J Clin Hypertens*. 2022;24:878–884. https://doi.org/10.1111/jch.14493