Published in final edited form as:

J Hypertens. 2019 March ; 37(3): 546–554. doi:10.1097/HJH.0000000000001909.

ARTERIAL STIFFNESS AND HYPERTENSION STATUS IN AFRO-CARIBBEAN MEN

Allison L KUIPERS, PhD¹, Iva MILJKOVIC, MD PhD¹, Emma BARINAS-MITCHELL, PhD¹, Ryan CVEJKUS, MS¹, Clareann H BUNKER, PhD¹, Victor W WHEELER, MBBS, MRCOG², and Joseph M ZMUDA, PhD¹

¹Department of Epidemiology, University of Pittsburgh, Pittsburgh, PA, USA;

²Tobago Health Studies Office, Scarborough, Tobago, Trinidad & Tobago

Abstract

Objective: African ancestry individuals are at high risk for hypertensive cardiovascular disease (CVD) and could benefit from early detection of arterial stiffening. We tested the association between the 2017 ACC/AHA hypertension categorizations, which include new blood pressure (BP) cutoffs and a definition for elevated BP, and arterial stiffness in 772 Afro-Caribbean men aged 50+ years (mean 64 years).

Methods: Arterial stiffness was assessed by brachial-ankle pulse-wave velocity (PWV) using a waveform analyzer. Hypertension groups were based on the 2017 ACC/AHA guidelines and by pharmacologic control status. Multiple linear/logistic regression was used to determine the association of PWV with BP and hypertension.

Results: Mean(SD) PWV was 1609(298) cm/s and was independently correlated with age, systolic BP, pulse, diabetes, height, and alcohol intake (all $P < 0.02$). After adjusting for these, in men aged ≥ 65 years, those with stage 1 or uncontrolled stage 2 hypertension had significantly greater PWV than all other groups (all $P < 0.05$). Men with controlled hypertension had similar PWV to those with elevated BP ($P = 0.7$); however, this was significantly greater than men with normal BP (all $P < 0.05$). Patterns were similar, but with smaller effect sizes, in men aged < 65 years (all $P < 0.05$ except controlled hypertension versus elevated or normal BP were not significant).

Conclusions: In these high-risk Afro-Caribbeans: 1) stage 1 hypertension is associated with increased PWV, which supports the new guidelines; and, 2) pharmacologic control appears to partially protect men from increased PWV. Longitudinal studies are needed to determine optimal PWV and timing of anti-hypertensive treatment for preventing future CVD.

CONDENSED ABSTRACT

This is the first study to test the association of arterial stiffness and hypertension in Afro-Caribbean men ($N = 772$, age = 50+ years). After adjusting for age, pulse, diabetes, height, and

Corresponding Author and Request for Reprints to: Allison L. Kuipers, PhD; Department of Epidemiology, Graduate School of Public Health, University of Pittsburgh; 130 DeSoto Street, A543 Crabtree Hall, Pittsburgh, PA 15261; kuipers@pitt.edu; Phone: 412-624-2781; Fax: 412-624-7397.

Conflicts of Interest:

The authors have no conflicts of interest to disclose.

alcohol intake, men aged 65 years with stage 1 or uncontrolled stage 2 hypertension had significantly greater PWV than all other men (all $P < 0.05$). Men with controlled hypertension or elevated BP (systolic 120–129 mmHg, diastolic < 80 mmHg) had greater PWV than men with normal BP (both $P < 0.05$). Patterns were similar with smaller effect sizes in men aged < 65 years (all $P < 0.05$ except controlled hypertension versus elevated or normal BP was not significant).

Keywords

arterial stiffness; blood pressure; hypertension; African ancestry; aging

INTRODUCTION

One of the vascular consequences of aging is increased arterial stiffness, which is caused by structural changes to the artery including fragmentation and degeneration of elastin, increases in collagen, extracellular matrix calcification, thickening of the arterial wall, and dilation of the arteries[1,2]. As arteries become stiffer and less compliant, the pulse wave velocity (PWV) and pulse pressure increases, leading to greater left ventricular afterload, which can result in isolated systolic hypertension, cardiac hypertrophy, decreased coronary perfusion, and/or microvascular damage[3,4]. These alterations in cardiac function can put an individuals at increased risk for myocardial infarction, heart failure, stroke, and kidney disease[3]. As such, increased blood pressure (BP) is both a cause and a consequence of arterial stiffening. Pulse wave velocity has been recognized as an important cardiovascular risk factor[5,6] with well-established validity, reliability, and clinical significance[7]. Pulse wave velocity also predicts 10-year cardiovascular events beyond traditional cardiovascular risk factors in the general population[8].

In a meta-analysis of the relationship of PWV to other traditional cardiovascular risk factors, age and BP were found to be consistently related to PWV[9]. The relationship of BP to increased PWV has been established as both an epidemiologic predictor[5,6,8,10] and a causal mechanism of the vascular structural changes that result in increased arterial stiffness[11]. Individuals with severe hypertension are likely to have clinically relevant arterial stiffening[4,9,11,12]; however, with the release of the 2017 ACC/AHA BP guidelines[13], it is important to investigate how arterial stiffness may vary in the newly defined, less-severe hypertension categories proposed by the ACC/AHA committee. Recently, multiple commentaries have been published on the global impact of the 2017 guidelines,[14,15] and suggest that there are still substantial gaps in knowledge about high blood pressure management in populations throughout the world where behavior and CVD outcomes may be different than in the US.

Individuals with African ancestry are at high risk for hypertension[16] with prevalence rates nearly 1.5-times greater than Caucasians in the US[17]. Additionally, measures of arterial stiffness, including PWV, appear to be worse in African ancestry individuals compared to Caucasians, even after adjustment for potential confounders[18,19]. The reason for this persistent racial difference is not known, but it is clear that hypertension and arterial stiffness are a particular concern for African ancestry populations, likely leading to their increased

risk of cerebrovascular disease and heart failure[20]. As such, these populations could be particularly benefited by early detection of significant arterial stiffness and interventions to slow the consequences of stiffening vessels. Therefore, in 772 Afro-Caribbean men from the Tobago Health Study, we aimed to determine the independent associations of correlates, including age, of PWV, and to test the arterial stiffness impact of the newly defined 2017 ACC/AHA BP categories compared to the previous hypertension definition. We hypothesized that men with the newly defined stage 1 or 2 hypertension would have greater PWV than men without hypertension, and that those in the intermediate ‘elevated BP’ group would have correspondingly intermediate PWV values. We also hypothesized that demonstration of pharmacologic control of hypertension would be associated with lower PWV.

METHODS

Tobago Health Study

All participants included in this analysis were from the Tobago Health Study (THS), a population-based, prospective cohort study of community-dwelling men aged 40 years and older, residing on the Caribbean island of Tobago[21]. The THS is a follow-up of the Tobago Prostate Cancer Study, which began in 1997 with the goal of providing screening and treatment for prostate cancer to the island’s male residents.[21] As such, there are only men in the THS and so the current analysis is in men only. Participants were recruited without regard to health status and men were eligible if they were ambulatory and not terminally ill. Men from Tobago are of African ancestry with low European admixture (<6%)[22]. The 772 men for the current analysis were recruited at a follow-up visit for the THS from 2014–2017 to have arterial stiffness measured via brachial-ankle pulse-wave velocity (baPWV). Clinical examinations and interviewer-administered health history questionnaires were administered at all THS visits. Written informed consent was obtained from each participant using forms and procedures approved by the University of Pittsburgh Institutional Review Board, the U.S. Surgeon General’s Human Use Review Board, and the Tobago Division of Health and Social Services Institutional Review Board.

Brachial-ankle Pulse-wave Velocity

Arterial stiffness was measured as brachial-ankle PWV (baPWV) using a non-invasive, waveform analyzer (Colin-VP1000, Omron, Japan/WaveNexus, TX) as previously described[23]. Briefly, following 10 minutes of rest in a supine position, occlusion/monitoring cuffs were placed at standardized locations on lightly clothed arms and bare ankles. Then, ECG electrodes were placed on the arms and ankles, while a phonocardiogram was placed on the left edge of the sternum to audibly detect heart sounds. The cuffs were connected to a plethysmographic sensor and an oscillometric pressure sensor, which recorded volume pressure waveforms and blood pressure, respectively. The volume pressure waveforms were collected at the arm (brachial artery) and ankle (tibial artery) over a total sampling time of 10 seconds with automatic gain analysis and quality adjustment. Brachial-ankle pulse-wave velocity was calculated as the (distance between arterial sites in cm) / (time between the foot of the waveforms in s). The distance was measured using a height based formula[7] that accounts for the opposite direction of blood flow by subtracting the

distance from the brachial artery to the heart. Mean baPWV was used in this analysis as the average between left and right baPWV measures. At the time of analysis, data from any participant with baPWV >2500 cm/s was considered potentially spurious[7] and was reviewed before being excluded from the current analysis (N=19), resulting in the final N of 772.

Hypertension Assessment

Blood pressure (BP) was measured using an automated sphygmomanometer (Omron) at the same clinic visit as the PWV assessment (BP measured first, then baPWV). As such, all potential exposures of interest (see *Other Characteristics* below) are the same for BP and PWV measures. Blood pressure was measured 3 times in a seated position with 10 minutes of rest in between readings, which is the protocol suggested by the 2017 guidelines[13] even though these data were collected before they were published. For this analysis, we present the mean of the 2nd and 3rd readings as average systolic and diastolic BP. Current use of antihypertension medications was assessed at the time of participant interview. For analyses of continuous BP measurements, we adjusted for antihypertensive therapy in order to control BP for any treatment effect. Hypertension was primarily defined using criteria that were standard at the time of the study examinations (2014–2017), which was mean systolic BP ≥ 140 mmHg, or diastolic BP ≥ 90 mmHg, or self-reported use of antihypertension medication. With the release of the 2017 ACC/AHA BP guidelines[13], we also defined hypertension using the newly defined categories of hypertension: 1) Normal BP: systolic BP <120 mmHg and diastolic BP <80 mmHg; 2) Elevated BP: systolic BP 120–129 mmHg and diastolic BP <80 mmHg; 3) Stage 1 Hypertension: systolic BP 130–139 mmHg or diastolic BP 80–89 mmHg; 4) Stage 2 Hypertension: systolic BP ≥ 140 mmHg or diastolic BP ≥ 90 mmHg. For our analyses, any men currently on antihypertensive medication were categorized as Stage 2 Hypertensive, regardless of BP measurement. Hypertension control for all analyses was defined at the time of study visit as any man on antihypertensive medication with average systolic BP <140 mmHg and diastolic BP <90 mmHg. We did not use the ACC/AHA-based definition of controlled hypertension because at the time of the THS study visit, medical guidelines only required the blood pressure to be <140/90 to be considered controlled.

Other Characteristics

Demographic, health history and anthropomorphic characteristics were assessed by trained staff using interview and clinical exams. Body weight was measured to the nearest 0.1 kg on a balance beam scale and standing height was measured to the nearest 0.1 cm using a wall-mounted stadiometer, both without participants wearing shoes. Body mass index was calculated as body weight in kilograms divided by standing height in meters squared. Waist circumference was measured at the level of the umbilicus or greatest circumference using a flexible tape measure (range 66–143cm). Fasting serum glucose was measured using an enzymatic procedure and fasting serum insulin was measured using a radioimmunoassay procedure developed by Linco Research, Inc. Diabetes was defined as a fasting serum glucose level ≥ 126 mg/dl, or current self-reported use of anti-diabetic medication. Current self-reported use of lipid-lowering therapies, including statins, as well as, other lipid-lowering medications, was assessed at the time of participant interview. Smoking status was

classified both as: 1) current or not, and 2) ever or not, wherein participants reporting smoking <100 cigarettes in their lifetime were considered never-smokers. Alcohol consumption is very limited in this cohort sample and was, therefore, coded as consuming >3 drinks per week (yes/no) to identify individuals with greater than average cohort alcohol intake. We modeled sedentary behavior as usually watching 14 hours of TV per week versus not.

Statistical Analysis

Brachial-ankle PWV was assessed for normality and transformed to a normal distribution using a log transformation. Means and standard deviations or frequencies were calculated for all variables of interest in the whole sample, and stratified by hypertension status. Differences in means or frequencies by hypertension status were tested using t-test or chi-square tests, as appropriate. Boxplots for baPWV were created for the whole sample and by 5-year age group, and the age effect was tested for a significant linear trend using linear regression.

All potential predictors of interest were tested for univariate association with baPWV using linear regression. Covariate effects are reported per 1 SD or 1-unit increase for continuous and categorical predictors, respectively. To determine the predictors with independent effects on baPWV, we used stepwise selection methods to select the model that explained the greatest amount of variance in baPWV. We included predictors with a univariate p-value <0.2 in the multivariable model and only kept those variables with a p-value <0.1 in the final model and forced in age. In order to control for possible multi-collinearity between various predictors during model selection, we only included the predictor(s) with the greatest univariate effects (as determined by linear regression R^2) given the following groupings: 1) body size: BMI, weight and height, waist circumference and height; 2) diabetes: fasting glucose and fasting insulin and antidiabetic medications, diabetes defined as yes/no, diabetes defined as yes/impaired fasting glucose/no; 3) hypertension: systolic BP and diastolic BP and antihypertensive medication, hypertension defined as yes/no. We adjusted any model that included continuous BP or glucose or insulin for the relevant medication in order to maintain adjustment for any treatment effect. Finally, we used backwards elimination methods[24] to verify the stepwise selection results.

Further analyses of baPWV stratified by age and/or hypertension status were conducted adjusting for all significant predictors using multiple linear regression models. We analyzed hypertension status using both the previously defined categories that were in place at the time of the THS exam, as well as, the 2017 ACC/AHA blood pressure guidelines in order to compare and contrast the importance of these new guidelines. Age was stratified at <65 or 65 years to determine general differences in these associations between younger or older adults. In all models, a P-value of 0.05 was considered statistically significant. All analyses were performed using SAS version 9.4 (Cary, NC, USA).

RESULTS

Characteristics of the Afro-Caribbean Men

Men in this analysis were aged 64 years on average (range 50–91 years; Table 1). Men were slightly overweight with a mean BMI of 28 kg/m² and a mean waist circumference of 98 cm. Twenty-two percent of men were diabetic, with 14% on lipid-lowering medication, 8% current smokers, and 14% had moderate alcohol intake. Sixty-two percent of men had hypertension, 67% of whom were on anti-hypertensive medication, but only 22.3% of hypertensive men had it under control. Hypertensives had greater age, BMI, waist circumference, and pulse rate, and were more likely to have diabetes and to report using lipid-lowering medications compared to non-hypertensives (all $P<0.05$, Table 1).

Association of baPWV with Age

Brachial-ankle PWV was 1609 cm/s on average (SD: 298 cm/s, range: 1000–2432 cm/s; Figure 1). Brachial-ankle PWV was significantly and strongly correlated with age ($r^2=0.464$, $P<0.0001$). Every 5-year greater age was associated with an 89 cm/s greater baPWV ($P<0.0001$; Figure 1) and all pair-wise comparisons of baPWV by 5-year age groups were significantly different ($P<0.05$) except the age 50–54 versus age 55–59 ($P=0.53$) and the age 70–74 versus age 75+ ($P=0.14$). The effect of age on baPWV was largely linear with only slight deviations at the tails of the age distribution where there were fewer observations, as shown by spline regression (Supplemental Figure 1).

Univariate Predictors of Arterial Stiffness in Afro-Caribbean Men

Univariate associations of potential clinical and demographic correlates of baPWV are shown in Table 2. Greater age, waist circumference, pulse rate, fasting glucose, systolic and diastolic BP, and lower height were associated with greater baPWV (all $P<0.05$). Additionally, diabetics, hypertensives, moderate drinkers, and men on antidiabetic, lipid-lowering, or antihypertensive medication had greater baPWV than men without those conditions (all $P<0.05$). Current smokers had lower baPWV ($P=0.01$), although a history of smoking was not associated with baPWV ($P=0.56$).

Multivariable Predictors of Arterial Stiffness in Afro-Caribbean Men

The final multivariable model containing only significant predictors of baPWV explained 42% of the variance in baPWV and included age, height, pulse rate, diabetes, alcohol intake, and systolic BP (all $P<0.05$; Table 2). We forced antihypertensive medication into the final multivariable model to adjust systolic BP for any treatment effect even though it was not a significant predictor of baPWV in the multivariable model ($P=0.42$). The strongest predictor of baPWV was age, which explained 12% of the variance. Every 1 SD (8.4 years) greater age was associated with 112 cm/s greater baPWV ($P<0.001$). The second strongest predictor of baPWV was systolic BP, which explained 10% of the variance, and every 1 SD (21.6 mmHg) greater systolic BP was associated with 102 cm/s higher baPWV ($P<0.001$). Pulse rate, diabetes, height, and alcohol intake each explained <5% of the variance in baPWV ($P<0.02$ for all).

Differences in Arterial Stiffness by Hypertension and Control Status using the Previous Hypertension Definition Guidelines

We stratified men by age (<65 years or ≥65 years) to determine differences in the patterns of mean baPWV by age and hypertension control status, after adjusting for all predictors in the final baPWV models except the BP-related predictors (systolic BP and antihypertensive medication; Figure 2A). Using the definition of hypertension from the THS clinic visit (systolic BP ≥140 mmHg or diastolic BP ≥90 mmHg or antihypertensive medication), baPWV was significantly greater in the older aged men compared to the younger aged men, regardless of hypertension or control status. Mean baPWV was similar in men without hypertension or with controlled hypertension and in both age groups. However, men with uncontrolled hypertension had a significant ~1/2SD greater baPWV compared to the other groups, in both ages ($P<0.01$ for all tests).

Differences in Arterial Stiffness by Hypertension and Control Status using the 2017 Hypertension Definition Guidelines

With the release of the 2017 ACC/AHA BP guidelines[13], we wanted to identify potential differences in mean baPWV in these new hypertension categories, as well as, by control status and age group (Figure 2B). Again after stratifying by age (<65 years or ≥65 years), in the older age group, the greatest baPWV was seen in men with newly defined ‘stage 1’ hypertension or uncontrolled ‘stage 2’ hypertension category, who had similar mean baPWV to each other ($P=0.65$). Additionally, men in the newly-defined ‘elevated BP’ category had similar baPWV to men with controlled hypertension ($P=0.73$), and that level was significantly greater than men without hypertension (both $P<0.02$).

In the younger age group, these trends were largely similar, though with less pronounced effect sizes. The most significant difference was that baPWV was greatest only in the men with uncontrolled ‘stage 2’ hypertension compared to all other groups ($P<0.0001$), though the ‘stage 1’ hypertension men also had greater baPWV compared to the ‘elevated BP’ and non-hypertensive men ($P<0.03$ for both). Brachial-ankle PWV was not significantly different in men with controlled hypertension compared to men without hypertension ($P=0.11$).

DISCUSSION

This is the first report to evaluate the status of arterial stiffness and hypertension in Afro-Caribbean men and to demonstrate the importance of the new, lower threshold hypertension categories with regard to arterial stiffness. In these men, greater age and blood pressure were strong independent predictors of baPWV, a validated measure of arterial stiffness, as were higher pulse rate, shorter height, diabetes, and moderate alcohol intake. Based on the previous definitions of hypertension that were in place at the time of the THS exam, we found that there was a high prevalence of hypertension (62%) in these men, but only 2/3 of hypertensives were on treatment, and <1/4 of all hypertensives had their BP controlled to systolic BP <140mmHg and diastolic BP <90mmHg.

Based on this sample of Afro-Caribbean men aged 50+ years recruited without regard to health status, 15% of men would be newly considered to be hypertensive (stage 1) based on

the 2017 ACC/AHA blood pressure guidelines (from 62% to 77%). However, this would only result in an estimated 2% of men benefitting from the addition of pharmacotherapy given the recommendation for lifestyle modification for most patients with stage 1 hypertension unless there is a previous history of CVD.[13] The major challenge for the Tobagonian population, given the new recommendations, would be to achieve adequate hypertension control, which is poor now and will be even more difficult to achieve as the BP target drops to 130/80 mmHg.

In general, the impact of the 2017 guidelines on hypertension prevalence in Tobago is very similar to the official report from the US, which estimates that the new guidelines would lead to a 14% increase in hypertension prevalence (from 32% to 46%) and an additional 2% of adults requiring additional pharmacological intervention.[25] However, the overall burden of hypertension in Afro-Caribbean men is notably higher than in the US, as a whole. Other members of the global community have also begun to explore the necessity of these US-based recommendations. For instance, in China, the new guidelines would add 17% to their hypertension prevalence, with 6% of elderly individuals requiring additional antihypertension pharmacotherapy.[26] Physicians in India[27] and Japan[28] are still debating the appropriateness of these guidelines in their countries. And Poulter *et al.*[15] note that given the low prevalence of hypertension control in many nations,[29] this may not be the appropriate time to impose more stringent guidelines. These discussions will no doubt continue throughout the global community in the coming years.

In the current study, we found that among Afro-Caribbean men aged 65 years or older, those who were classified into any of the three newly established high BP categories (stage 2 hypertension, stage 1 hypertension, or elevated BP) had significantly greater arterial stiffness than normotensive men. Men with stage 1 hypertension, who previously would have been considered pre-hypertensive, had statistically indistinguishable baPWV from men in the stage 2 hypertension group. However, men with controlled hypertension had significantly lower baPWV than either of the hypertensive groups, reinforcing the importance of adequate hypertension control for vascular health. Trends were similar though not always significant in the younger aged men (range 50–65 years). In particular, in these younger men, arterial stiffness was similarly low in three groups: those without hypertension, those with only elevated BP, and those with pharmacologically controlled hypertension. This suggests that in these younger age groups, proper identification and treatment of hypertension early may have a somewhat normalizing effect on arterial stiffness. Putting our results from both the younger and older age groups together, these findings support the conclusions drawn by the ACC/AHA task force in determining that a lower BP threshold should be considered optimal for maintaining a healthy vasculature throughout the aging process, though the feasibility of that is yet to be determined.

In addition to blood pressure, older age was a strong predictor of arterial stiffness, which is a known consequence of aging.[1,30] Increased arterial stiffness is thought to be an intermediary pathway between aging and a number of cardiovascular and aging conditions, including left ventricular dysfunction,[31,32] heart failure,[5,33] cognitive decline,[34–37] and even Alzheimer's Disease.[34] While the THS men are young enough to have very few

of these conditions, African ancestry individuals are known to suffer disproportionately from hypertensive vascular diseases.[20]

Other correlates of baPWV in this study were similar to those seen in previous studies in African ancestry subjects,[19,38–43] and included pulse rate, diabetes, height, and alcohol intake. Pulse rate and height are known correlates of PWV as they are related to the size and anatomic structure of the vasculature, which is a major component of the arterial pressure wave and PWV calculation.[44] Diabetes is also a known correlate of arterial stiffness,[19,38–43] which is thought to partially be due to insulin's ability to stimulate the sympathetic nervous system, resulting in elevated BP and PWV.[45,46] Measures of adiposity were not independently associated with baPWV, even though previous studies[43,47–51] have suggested that obesity and/or greater ectopic fat are associated with arterial stiffness. However, little of this previous research has been conducted in African ancestry men. Additionally, while moderate alcohol intake is often considered a protective factor for cardiovascular disease,[52] it was a risk factor for increased baPWV in these men. There is low alcohol intake in Tobago, generally, with 59% of THS men reporting no alcohol intake in an average week. It is possible that cultural differences in alcohol consumption may underlie this differential direction of effect. However, at least one other study has reported that alcohol intake is associated with greater baPWV in Blacks,[53] suggesting there may be a racial difference in the effect of alcohol intake on arterial stiffness.

This is the first study of the impact of the 2017 ACC/AHA BP guidelines on arterial stiffness, and is one of the first studies on arterial stiffness in Afro-Caribbeans. Our findings support the idea for a potential increased risk of some vascular and cardiac complications in individuals with a BP $\geq 130/80$ mmHg. We used the gold standard method for measuring BP including having the participant seated, measuring BP 3 times, and including at least 10 minutes of rest between measurements. However, the current analysis is cross-sectional, and as such, cannot determine the temporality of the association, although previous studies have suggested hypertension does increase arterial stiffness.[3] Longitudinal studies will be required to determine exactly which BP threshold should be considered ideal for maintaining compliant arteries as long as possible through the aging process. Additionally, we were able to explain 42% of the variance in arterial stiffness in these Afro-Caribbean men with limited of traditional CVD risk factors, including the large contribution from aging and blood pressure. However, we were not able to investigate the association of any biochemical or molecular markers of CVD risk, such as lipid and lipoprotein measures, inflammatory factors, or endothelial function markers, with arterial stiffness.

In these Afro-Caribbean men who are at high-risk for hypertensive vascular disease, arterial stiffness was strongly correlated with aging and blood pressure, even in the 2017 ACC/AHA BP categories. Men with the newly defined stage 1 hypertension category, who would not have previously been considered hypertensive, had similar stiffness as the previously defined stage 2 hypertension, reinforcing the ACC/AHA's recommendation for this new category of risk. Our findings also highlight the importance of adequate hypertension control in this population for limiting the effects of high blood pressure and arterial stiffness on the vasculature, as suggested previously[54]. Hypertension control will continue to be an important clinical outcome to follow as the 2017 guidelines drop the threshold from 140/90

to 130/80 mmHg, especially in these Afro-Caribbean men who have poor control even at the higher threshold. Future longitudinal studies in diverse populations will be informative for investigating if the optimal blood pressure thresholds presented in the 2017 guidelines are reasonable for all race/ethnicities, as well as, to determine the best timing and treatment plan for hypertension in order to slow arterial stiffness progression and minimize future CVD risk.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

ACKNOWLEDGEMENTS

The authors would like to thank all supporting staff from the Tobago Health Study Office and University of Pittsburgh Ultrasound Research Lab.

Sources of Funding:

This work was supported by grant K01-HL125658 (PI: Kuipers) from the National Heart, Lung and Blood Institute, and by grant R01-DK097084 (PI: Miljkovic) from the National Institute of Diabetes and Digestive and Kidney Diseases. The data presented within this manuscript have not been presented previously, either in full or in part.

REFERENCES

1. Lakatta EG. Arterial and cardiac aging: major shareholders in cardiovascular disease enterprises: Part III: cellular and molecular clues to heart and arterial aging. *Circulation* 2003; 107 (3):490–497. [PubMed: 12551876]
2. Safar ME. Epidemiological aspects of pulse pressure and arterial stiffness. *J Hypertens Suppl* 1999; 17 (5):S37–40.
3. Palombo C, Kozakova M. Arterial stiffness, atherosclerosis and cardiovascular risk: Pathophysiologic mechanisms and emerging clinical indications. *Vascul Pharmacol* 2016; 77:1–7. [PubMed: 26643779]
4. Najjar SS, Scuteri A, Shetty V, Wright JG, Muller DC, Fleg JL, et al. Pulse wave velocity is an independent predictor of the longitudinal increase in systolic blood pressure and of incident hypertension in the Baltimore Longitudinal Study of Aging. *Journal of the American College of Cardiology* 2008; 51 (14):1377–1383. [PubMed: 18387440]
5. Sutton-Tyrrell K, Najjar SS, Boudreau RM, Venkitachalam L, Kupelian V, Simonsick EM, et al. Elevated aortic pulse wave velocity, a marker of arterial stiffness, predicts cardiovascular events in well-functioning older adults. *Circulation* 2005; 111 (25):3384–3390. [PubMed: 15967850]
6. Vlachopoulos C, Aznaouridis K, Stefanadis C. Prediction of cardiovascular events and all-cause mortality with arterial stiffness: a systematic review and meta-analysis. *Journal of the American College of Cardiology* 2010; 55 (13):1318–1327. [PubMed: 20338492]
7. Yamashina A, Tomiyama H, Takeda K, Tsuda H, Arai T, Hirose K, et al. Validity, reproducibility, and clinical significance of noninvasive brachial-ankle pulse wave velocity measurement. *Hypertension research : official journal of the Japanese Society of Hypertension* 2002; 25 (3):359–364. [PubMed: 12135313]
8. Hansen TW, Staessen JA, Torp-Pedersen C, Rasmussen S, Li Y, Dolan E, et al. Ambulatory arterial stiffness index predicts stroke in a general population. *J Hypertens* 2006; 24 (11):2247–2253. [PubMed: 17053547]
9. Cecelja M, Chowienczyk P. Dissociation of aortic pulse wave velocity with risk factors for cardiovascular disease other than hypertension: a systematic review. *Hypertension* 2009; 54 (6): 1328–1336. [PubMed: 19884567]

10. Vlachopoulos C, Aznaouridis K, Terentes-Printzios D, Ioakeimidis N, Stefanadis C. Prediction of cardiovascular events and all-cause mortality with brachial-ankle elasticity index: a systematic review and meta-analysis. *Hypertension* 2012; 60 (2):556–562. [PubMed: 22733468]
11. Blacher J, Safar ME. Large-artery stiffness, hypertension and cardiovascular risk in older patients. *Nature clinical practice Cardiovascular medicine* 2005; 2 (9):450–455.
12. Tomiyama H, Arai T, Koji Y, Yambe M, Motobe K, Zaydun G, et al. The age-related increase in arterial stiffness is augmented in phases according to the severity of hypertension. *Hypertension research : official journal of the Japanese Society of Hypertension* 2004; 27 (7):465–470. [PubMed: 15302982]
13. Whelton PK, Carey RM, Aronow WS, Casey DE, Jr., Collins KJ, Dennison Himmelfarb C, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Hypertension* 2017.
14. Lackland DT, Beilin LJ, Campbell NRC, Jaffe MG, Orlas M, Ram CV, et al. Global Implications of Blood Pressure Thresholds and Targets: Guideline Conversations From the World Hypertension League. *Hypertension* 2018; 71 (6):985–987. [PubMed: 29686002]
15. Poulter NR, Castillo R, Charchar FJ, Schlaich MP, Schutte AE, Tomaszewski M, et al. Are the American Heart Association/American College of Cardiology High Blood Pressure Guidelines Fit for Global Purpose?: Thoughts From the International Society of Hypertension. *Hypertension* 2018.
16. Flack JM, Sica DA, Bakris G, Brown AL, Ferdinand KC, Grimm RH, et al. Management of High Blood Pressure in Blacks. An Update of the International Society on Hypertension in Blacks Consensus Statement 2010; 56 (5):780–800.
17. Lackland DT. Racial differences in hypertension: implications for high blood pressure management. *Am J Med Sci* 2014; 348 (2):135–138. [PubMed: 24983758]
18. Li S, Chen W, Srinivasan SR, Berenson GS. Influence of metabolic syndrome on arterial stiffness and its age-related change in young adults: the Bogalusa Heart Study. *Atherosclerosis* 2005; 180 (2):349–354. [PubMed: 15910862]
19. Strain WD, Chaturvedi N, Dockery F, Shiff R, Shore AC, Bulpitt CJ, et al. Increased arterial stiffness in Europeans and African Caribbeans with type 2 diabetes cannot be accounted for by conventional cardiovascular risk factors. *American journal of hypertension* 2006; 19 (9):889–896. [PubMed: 16942929]
20. Lloyd-Jones D, Adams RJ, Brown TM, Carnethon M, Dai S, De Simone G, et al. Heart disease and stroke statistics—2010 update: a report from the American Heart Association. *Circulation* 2010; 121 (7):e46–e215. [PubMed: 20019324]
21. Hill DD, Cauley JA, Sheu Y, Bunker CH, Patrick AL, Baker CE, et al. Correlates of bone mineral density in men of African ancestry: the Tobago bone health study. *Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA* 2008; 19 (2):227–234.
22. Miljkovic-Gacic I, Ferrell RE, Patrick AL, Kammerer CM, Bunker CH. Estimates of African, European and Native American ancestry in Afro-Caribbean men on the island of Tobago. *Hum Hered* 2005; 60 (3):129–133. [PubMed: 16282694]
23. Venkitachalam L, Mackey RH, Sutton-Tyrrell K, Patel AS, Boraz MA, Simkin-Silverman LR, et al. Elevated pulse wave velocity increases the odds of coronary calcification in overweight postmenopausal women. *American journal of hypertension* 2007; 20 (5):469–475. [PubMed: 17485005]
24. Halinski RS, Feldt LS. The selection of variables in multiple regression analysis. *Journal of Educational Measurement* 1970; 7 (3):151–158.
25. Muntner P, Carey RM, Gidding S, Jones DW, Taler SJ, Wright JT, Jr., et al. Potential US Population Impact of the 2017 ACC/AHA High Blood Pressure Guideline. *Circulation* 2018; 137 (2):109–118. [PubMed: 29133599]

26. Wang JG, Liu L. Global Impact of 2017 American College of Cardiology/American Heart Association Hypertension Guidelines: A Perspective From China. *Circulation* 2018; 137 (6):546–548. [PubMed: 29431657]
27. Wander GS, Ram CVS. Global Impact of 2017 American Heart Association/American College of Cardiology Hypertension Guidelines: A Perspective From India. *Circulation* 2018; 137 (6):549–550. [PubMed: 29431658]
28. Kario K Global Impact of 2017 American Heart Association/American College of Cardiology Hypertension Guidelines: A Perspective From Japan. *Circulation* 2018; 137 (6):543–545. [PubMed: 29431656]
29. Chow CK, Teo KK, Rangarajan S, Islam S, Gupta R, Avezum A, et al. Prevalence, awareness, treatment, and control of hypertension in rural and urban communities in high-, middle-, and low-income countries. *Jama* 2013; 310 (9):959–968. [PubMed: 24002282]
30. Scuteri A, Morrell CH, Orru M, Strait JB, Tarasov KV, Ferrelli LA, et al. Longitudinal perspective on the conundrum of central arterial stiffness, blood pressure, and aging. *Hypertension* 2014; 64 (6):1219–1227. [PubMed: 25225210]
31. Fernandes VR, Polak JF, Cheng S, Rosen BD, Carvalho B, Nasir K, et al. Arterial stiffness is associated with regional ventricular systolic and diastolic dysfunction: the Multi-Ethnic Study of Atherosclerosis. *Arteriosclerosis, thrombosis, and vascular biology* 2008; 28 (1):194–201.
32. Libhaber E, Woodiwiss AJ, Libhaber C, Maseko M, Majane OH, Makaula S, et al. Gender-specific brachial artery blood pressure-independent relationship between pulse wave velocity and left ventricular mass index in a group of African ancestry. *J Hypertens* 2008; 26 (8):1619–1628. [PubMed: 18622241]
33. Pandey A, Khan H, Newman AB, Lakatta EG, Forman DE, Butler J, et al. Arterial Stiffness and Risk of Overall Heart Failure, Heart Failure With Preserved Ejection Fraction, and Heart Failure With Reduced Ejection Fraction: The Health ABC Study (Health, Aging, and Body Composition). *Hypertension* 2017; 69 (2):267–274. [PubMed: 27993954]
34. Scuteri A, Stone J, O'Rourke MF. The relationship between aortic stiffness, microvascular disease in the brain and cognitive decline: Insights into the emerging epidemic of Alzheimer's Disease. In: Safar ME, editor. *Blood Pressure and Arterial Wall Mechanics in Cardiovascular Diseases* London: Springer-Verlag; 2014 pp. 307–320.
35. Scuteri A, Tesaro M, Appolloni S, Preziosi F, Brancati AM, Volpe M. Arterial stiffness as an independent predictor of longitudinal changes in cognitive function in the older individual. *J Hypertens* 2007; 25 (5):1035–1040. [PubMed: 17414668]
36. Scuteri A, Tesaro M, Guglini L, Lauro D, Fini M, Di Daniele N. Aortic stiffness and hypotension episodes are associated with impaired cognitive function in older subjects with subjective complaints of memory loss. *International journal of cardiology* 2013; 169 (5):371–377. [PubMed: 24120214]
37. Scuteri A, Wang H. Pulse wave velocity as a marker of cognitive impairment in the elderly. *J Alzheimers Dis* 2014; 42 Suppl 4:S401–410. [PubMed: 25182740]
38. Cruickshank JK, Silva MJ, Molaodi OR, Enayat ZE, Cassidy A, Karamanos A, et al. Ethnic Differences in and Childhood Influences on Early Adult Pulse Wave Velocity: The Determinants of Adolescent, Now Young Adult, Social Wellbeing, and Health Longitudinal Study. *Hypertension* 2016; 67 (6):1133–1141. [PubMed: 27141061]
39. Loehr LR, Meyer ML, Poon AK, Selvin E, Palta P, Tanaka H, et al. Prediabetes and Diabetes Are Associated With Arterial Stiffness in Older Adults: The ARIC Study. *American journal of hypertension* 2016; 29 (9):1038–1045. [PubMed: 27068705]
40. Park CM, Tillin T, March K, Jones S, Whincup PH, Mayet J, et al. Adverse effect of diabetes and hyperglycaemia on arterial stiffness in Europeans, South Asians, and African Caribbeans in the SABRE study. *J Hypertens* 2016; 34 (2):282–289. [PubMed: 26628109]
41. Scuteri A, Cunha PG, Rosei EA, Badariere J, Bekaert S, Cockcroft JR, et al. Arterial stiffness and influences of the metabolic syndrome: a cross-countries study. *Atherosclerosis* 2014; 233 (2):654–660. [PubMed: 24561493]

42. Shoji T, Emoto M, Shinohara K, Kakiya R, Tsujimoto Y, Kishimoto H, et al. Diabetes mellitus, aortic stiffness, and cardiovascular mortality in end-stage renal disease. *Journal of the American Society of Nephrology* : JASN 2001; 12 (10):2117–2124. [PubMed: 11562410]
43. Sutton-Tyrrell K, Newman A, Simonsick EM, Havlik R, Pahor M, Lakatta E, et al. Aortic stiffness is associated with visceral adiposity in older adults enrolled in the study of health, aging, and body composition. *Hypertension* 2001; 38 (3):429–433. [PubMed: 11566917]
44. Van Bortel LM, Struijker-Boudier HA, Safar ME. Pulse pressure, arterial stiffness, and drug treatment of hypertension. *Hypertension* 2001; 38 (4):914–921. [PubMed: 11641309]
45. DeFronzo RA, Ferrannini E. Insulin resistance. A multifaceted syndrome responsible for NIDDM, obesity, hypertension, dyslipidemia, and atherosclerotic cardiovascular disease. *Diabetes Care* 1991; 14 (3):173–194. [PubMed: 2044434]
46. King GL, Wakasaki H. Theoretical mechanisms by which hyperglycemia and insulin resistance could cause cardiovascular diseases in diabetes. *Diabetes Care* 1999; 22 Suppl 3:C31–37. [PubMed: 10189560]
47. van den Munckhof ICL, Holewijn S, de Graaf J, Rutten JHW. Sex differences in fat distribution influence the association between BMI and arterial stiffness. *J Hypertens* 2017; 35 (6):1219–1225. [PubMed: 28441693]
48. Diemer FS, Brewster LM, Haan YC, Oehlers GP, van Montfrans GA, Nahar-van Venrooij LMW. Body composition measures and cardiovascular risk in high-risk ethnic groups. *Clinical nutrition* (Edinburgh, Scotland) 2017.
49. Al-Talabany S, Mordi I, Graeme Houston J, Colhoun HM, Weir-McCall JR, Matthew SZ, et al. Epicardial adipose tissue is related to arterial stiffness and inflammation in patients with cardiovascular disease and type 2 diabetes. *BMC Cardiovasc Disord* 2018; 18 (1):31. [PubMed: 29433433]
50. Lee HJ, Kim HL, Chung J, Lim WH, Seo JB, Kim SH, et al. Interaction of Metabolic Health and Obesity on Subclinical Target Organ Damage. *Metabolic syndrome and related disorders* 2018; 16 (1):46–53. [PubMed: 29319402]
51. Hughes TM, Althouse AD, Niemczyk NA, Hawkins MS, Kuipers AL, Sutton-Tyrrell K. Effects of weight loss and insulin reduction on arterial stiffness in the SAVE trial. *Cardiovasc Diabetol* 2012; 11:114. [PubMed: 22998737]
52. Toma A, Pare G, Leong DP. Alcohol and Cardiovascular Disease: How Much is Too Much? *Curr Atheroscler Rep* 2017; 19 (3):13. [PubMed: 28210975]
53. Maritz M, Fourie CMT, van Rooyen JM, Kruger IM, Schutte AE. A health profile associated with excessive alcohol use independently predicts aortic stiffness over 10 years in black South Africans. *J Hypertens* 2017; 35 (11):2268–2275. [PubMed: 28665888]
54. Guo J, Fujiyoshi A, Masaki K, Vishnu A, Kadota A, Barinas-Mitchell EJ, et al. The role of initial and longitudinal change in blood pressure on progression of arterial stiffness among multiethnic middle-aged men. *J Hypertens* 2017; 35 (1):111–117. [PubMed: 27775956]

Figure 1. Boxplots of Arterial Stiffness by Age in Afro-Caribbean Men

Boxplots of baPWV are shown in all men (left) and by 5-year age groups from age 50 years to age 75+ years (right). As the plots show, baPWV is higher with older age (P for trend <0.0001).

Figure 2. Multivariable Adjusted Mean(SE) Differences in Arterial Stiffness by Age, and Hypertension Category and Control Status in Afro-Caribbean Men

The figure shows multivariable adjusted means and SE (standard error bars) for baPWV stratified by age and hypertension status adjusted for age, height, pulse rate, diabetes, and alcohol intake. Panel A shows adjusted mean baPWV using the hypertension definition (systolic BP ≥ 140 mmHg, or diastolic BP ≥ 90 mmHg, or antihypertensive medication) at the time of the exam. Panel B shows adjusted mean baPWV using the newly released, 2017 ACC/AHA BP Categorizations[13] (Elevated BP: systolic BP 120–129 mmHg AND diastolic BP <80 mmHg; Stage 1 Hypertension: systolic BP 130–139 mmHg OR diastolic BP 80–89 mmHg; Stage 2 Hypertension: systolic BP ≥ 140 mmHg OR diastolic BP ≥ 90 mmHg). Both panels also show means for hypertension control which was defined as any man on antihypertensive medication with average systolic BP <140 mmHg AND diastolic BP <90 mmHg.

Table 1.Characteristics^{*} of the 772 Afro-Caribbean Men by Hypertension[#] Status

	Overall (N=772)	No Hypertension (N=292)	Hypertension (N=480)	P-value [§]
Age (years)	63.6±8.4	61.2±7.2	65.1±8.7	<0.001
BMI (kg/m ²)	27.7±4.5	26.2±4.2	28.5±4.5	<0.001
Weight (kg)	85.0±15.4	80.6±13.9	87.6±15.6	<0.001
Height (cm)	175.1±6.7	175.1±6.2	175.1±6.9	0.977
Waist Circumference (cm)	98.3±12.6	94.0±11.3	100.9±12.6	<0.001
Pulse (beat/min)	67.5±11.9	65.1±11.2	69.0±12.0	<0.001
Fasting Glucose (mg/dL)	100.7±38.8	94.7±36.3	104.3±39.9	<0.001
Fasting Insulin (μU/mL)	11.7±10.8	8.9±6.1	12.4±12.6	<0.001
Impaired fasting glucose (%)	10.3	8.6	11.4	0.026
Diabetes (%)	22.3	11.7	28.8	<0.001
Antidiabetic Medication (%)	17.8	8.2	23.5	<0.001
Lipid-lowering Therapy (%)	13.5	3.8	19.4	<0.001
Current Smoking (%)	8.3	10.6	6.9	0.069
Previous Smoking (%)	19.8	17.1	21.5	0.139
>3 alcoholic drinks/week (%)	13.5	12.0	14.4	0.346
Watch>14 hrs TV/week (%)	49.1	44.9	51.7	0.067
Walked in last week (hours)	3.2±4.3	3.6±4.4	2.9±4.3	0.053
Systolic BP (mmHg)	142.2±21.6	125.5±9.7	152.3±20.5	<0.001
Diastolic BP (mmHg)	79.5±12.1	71.6±8.0	84.3±11.7	<0.001
Anytihypertensive Medication (%)	41.6	N/A	66.9	N/A
Controlled Hypertension (%)	13.9	N/A	22.3	N/A

^{*} Characteristics shown as mean±SD or %, as appropriate.[#] Hypertension was defined at the time of clinical exam as systolic BP ≥140mmHg or diastolic BP ≥90mmHg or interviewer-confirmed current use of antihypertensive medication.[§] P-value shown for the t-test or chi-square test of a difference in mean or frequency, respectively, by hypertension status.

Table 2.

Correlates of Arterial Stiffness in Afro-Caribbean Men

	Unit [*]	Univariate Models [*]		Final Multivariable Model [*] (Model R ² : 0.424)		
		Beta	P-value	Beta	P-value	Predictor R ²
Age	8.4	137.59	<0.001	112.24	<0.001	0.121
BMI	4.5	-5.76	0.878			
Weight	15.4	-24.96	0.053			
Height	6.7	-45.61	<0.001	-28.33	0.001	0.008
Waist Circumference	12.6	18.41	0.043			
Pulse	11.9	65.26	<0.001	49.65	<0.001	0.030
Fasting Glucose	38.8	36.73	0.001			
Fasting Insulin	10.8	3.39	0.6727			
Diabetes (no/yes)	1	152.04	<0.001			
Diabetes (no/IFG/yes)	1	78.44	<0.001	44.73	<0.001	0.015
Antidiabetic Meds	1	150.83	<0.001			
Lipid-lowering Therapy	1	87.37	0.008			
Current Smoking	1	-94.06	0.011			
Previous Smoking	1	16.81	0.563			
>3 alcoholic drinks/week	1	70.06	0.024	59.95	0.016	0.006
Watch>14 hrs TV/week	1	14.45	0.4692			
Hours walked last week	4.3	-14.00	0.253			
Systolic BP	21.6	133.79	<0.001	101.88	<0.001	0.103
Diastolic BP	12.1	77.25	<0.001			
Hypertension	1	214.05	<0.001			
Antihypertensive Meds [#]	1	150.44	<0.001	13.63	0.424	0.001

^{*} All effects are modeled per 1 SD or 1 unit for each continuous and categorical variable, respectively. Univariate models were modeled individually using linear regression. The final multivariable model was selected using model selection procedures to maximize the variance explained by multiple predictors within a single model. Predictors with multivariable P-value<0.1 were kept in the model. See the methods section for more detail on statistical modeling.

[#] Antihypertensive medication was forced into the final multivariable model to control systolic BP for any treatment effect.