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ARTICLE

Comparing the associations of clinic vs. ambulatory blood pressure with subclinical organ damage in young healthy adults: the African-PREDICT study

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Abstract

Raised blood pressure (BP) causes pathophysiological cardiovascular changes resulting in target organ damage. Although ambulatory and central BP relate more strongly to outcomes than clinical brachial BP in the elderly population, it is unknown which measure of BP is most strongly associated with markers of organ damage in younger populations. We compared the strength of associations between different BPs and measures of subclinical organ damage and investigated whether ethnic differences exist between these associations. The design was a cross-sectional analysis of the African-PREDICT study, including young black and white men and women (aged 20–30, $N = 1202$). We obtained clinic, ambulatory, and central BP readings, as well as measures of subclinical organ damage: central retinal arteriolar equivalent (CRAE) from fundus images, echocardiography to determine left ventricular mass index (LVMi), carotid intima media thickness (CIMT), carotid-femoral pulse wave velocity (PWV), and albumin-to-creatinine ratio (ACR) determined from spot urine samples. Overall, weak correlations were evident between CIMT, ACR, and BP, whereas CRAE, LVMi, and PWV correlated strongly with BP. In the total group, clinic brachial BP had stronger associations with CRAE, LVMi, and PWV (all $p < 0.001$) than ambulatory and central BP. Although the ethnic groups showed similar correlations between CRAE, LVMi, CIMT, and the various BPs, PWV correlated more strongly with ambulatory systolic BP ($p < 0.001$) in white participants. In young healthy adults, clinic brachial BP correlated more strongly with measures of early target organ damage than central or ambulatory BP. No differences were observed between correlations of BP and measures of target organ damage in the two ethnic groups.

Keywords Blood pressure · Target organ damage · Ethnicity

Introduction

Hypertension is the leading cause of mortality globally, with 10.4 million deaths reported per annum [1]. Raised blood pressure reflects pathophysiological changes within the cardiovascular system resulting in target organ damage. These changes occurring in the cardiovascular system are predictors of cardiovascular morbidity and mortality [2]. Pathophysiological changes may occur throughout the cardiovascular system: the microvasculature (typically retinal arteriolar narrowing) [3], large artery structure and function (increased carotid wall thickness and large artery stiffness) [4], the heart (through an increase in left ventricular mass) [5], and the kidneys (detected by microalbuminuria) [6, 7].

Brachial blood pressure measured in the clinic remains the standard and most widely used method of measurement because of the ease of accessibility, simple method, and

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cost-effectiveness [8]. However, 24-h ambulatory blood pressure is the gold standard for measuring blood pressure (BP) [2] due to its better prognostic value and its ability to reflect nighttime BP, which is a strong predictor of morbidity and mortality [9, 10]. Several measurements reflecting central hemodynamics, including central systolic blood pressure and central pulse pressure, show stronger associations with cardiovascular events and mortality [9–15] than office brachial blood pressure. Central pulse pressure is generally regarded as a surrogate of large artery stiffness in older individuals [16, 17].

As previous studies focused on the associations between different BP measurements and organ damage, morbidity, and mortality in older or diseased populations [9–15, 18–20], it is unclear whether similar relationships are apparent during the early manifestation of cardiovascular disease in young healthy adults. In addition, when taking different ethnic groups into account, a higher prevalence of increased BP was reported in black populations than in white populations, with resultant increased cardiovascular disease and mortality [21–23]. Studies comparing black and white ethnic groups found that black populations showed elevated central, brachial, and nighttime systolic and diastolic BP compared to white populations. This increase in BP may be due to early endothelial dysfunction, increased vascular tone, microvascular structural changes, and an increase in the stiffening of the aorta [22]. Previous studies have also indicated an increased prevalence of left ventricular hypertrophy and early vascular aging in black population groups [22, 24–27]. Whether any ethnic differences exist between measures of BP and subclinical organ damage in young populations remains unclear. We therefore aimed to compare the strength of associations between different BP estimates (clinical [brachial and central] and ambulatory BP) with measures of subclinical organ damage in young adults and to determine whether there are ethnic differences in the strength of these correlations.

Methods

Study design and population

The study is part of the African Prospective study on the Early Detection and Identification of Cardiovascular disease and Hypertension (African-PREDICT) [28]. The central aim of African-PREDICT is to follow young, apparently healthy adults over a 10-year period to identify novel markers related to early cardiovascular disease development. This substudy included cross-sectional data from the full baseline cohort of 1202 participants, for which data collection took place from 2013 to 2017.

Participants were recruited from Potchefstroom (South Africa) and the surrounding areas by field workers, via their workplace, or through advertisement by means of local newspapers or radio stations. Participants were initially screened, and those who met the criteria were included in the study. The inclusion criteria were young (20–30 years), apparently healthy black and white men and women with a normal screening clinic BP (<140/90 mmHg), free from human immunodeficiency virus infection, no self-reported chronic disease (or treatment thereof), and not pregnant or breastfeeding at the time of inclusion. The study was approved by the Health Research Ethics Committee of the North-West University, and every participant gave written informed consent.

Questionnaires

Participants completed the General Health and Demographic Questionnaire online on a web-based program that captured basic information such as sex, age, socioeconomic status, alcohol and tobacco usage, and medication use.

Anthropometric measurements

Standard procedures were used to determine height (SECA 213 Portable Stadiometer, SECA, Hamburg, Germany), weight (SECA 813 Electronic Scales, SECA, Hamburg, Germany), and waist circumference (WC) (Lufkin Steel Anthropometric Tape (W606PM) Lufkin, Apex, USA). Body mass index (BMI) was calculated.

Cardiovascular measurements

Blood pressure measurements

With the use of the Dinamap Procare 100 Vital Signs Monitor (GE Medical Systems, Milwaukee, USA), the clinic brachial blood pressure of participants was measured. Before the measurement was conducted, participants were requested to refrain from eating, smoking, and exercise for at least 30 min beforehand and to be seated in a resting state with the arms supported at heart level. After the participant was seated calmly for 5 min, the first measurement was taken on the left arm. Blood pressure was measured on the right arm in duplicate. A final measurement was then made on the left upper arm of the participant. The SBP, DBP, and heart rate were captured after each measurement. For data analyses, the mean of all four BP measurements was used.

Twenty-four-hour ambulatory blood pressure monitoring (ABPM) was measured using a validated [29] 24-h ABPM apparatus (Card(X)plore, Meditech, Budapest, Hungary). The participant was fitted with an appropriately sized cuff on the nondominant arm and was given instructions on how

to ensure successful inflation of the 24-h ABPM apparatus over the 24-h time period. The ABPM apparatus was programmed to measure BP at intervals of 30 min during the day (06:00–22:00) and hourly at night (22:00–06:00). Participants were given an ambulatory diary card that they completed during the 24-h duration of the measurement. For the total sample of participants, the mean successful inflation rate was 88.0 ± 12.4%.

Central systolic blood pressure was measured by performing pulse wave analysis using a SphygmoCor® XCEL device (AtCor Medical Pty. Ltd., Sydney, Australia). A brachial cuff was placed on the right upper arm with the participant in the supine position. A general transfer function was used to estimate central systolic pressure. The measurement was performed in duplicate.

Assessment of subclinical organ damage

Microvascular calibers were evaluated through static retinal images using the dynamic retinal vessel analyzer. Fifteen to thirty minutes before the measurement, the participant was administered a drop of tropicamide (1% Alcon) in the right eye by a registered nurse to induce mydriatic conditions. Monochrome and color retinal images were captured using Visualis 2.81 software at a 50° camera angle. These images underwent vessel analysis using VesselMap2 software. Vessels located between 0.5 and 2 optic disc diameters from the outer margin of the optic disc were marked either as arteries or veins. The central retinal arteriolar caliber (CRAE) was calculated using the Knudtson formula [30], and only the six largest arteries were included in the formula. CRAE was measured in measuring units (MU), where 1 MU is equivalent to 1 μM if the dimensions of the eye are similar to those of the normal Gullstrand eye.

The echocardiography procedure was conducted by a medical clinical technologist while the participant was in a partial left decubitus position with the head elevated. A General Electric Vivid E9 device (GE Vingmed Ultrasound A/S, Horten, Norway) was used with a 2.5–3.5-MHz transducer and a single ECG lead for timing purposes. Left ventricular mass index (LVMi) was calculated, and abnormal LVMi was estimated by the Deveraux equation [31] previously developed in a population of normal-weight, normotensive adults between 18 and 85 years of age [21].

Carotid intima media thickness (cIMT) measurements were made by a single sonographer on the left and right common carotid arteries as well as the internal carotid artery using a General Electric Vivid E9 device (GE Vingmed Ultrasound A/S, Horten, Norway). Each side was measured and recorded for similar future assessments from various optimal angles. The images were digitized and analyzed using Artery Measurement Systems software (Gustavvson, Sweden).

Arterial stiffness was assessed noninvasively and in duplicate by trained researchers according to the manufacturer's instructions to determine carotid-femoral pulse wave velocity (PWV) using a SphygmoCor® XCEL device (AtCor Medical Pty. Ltd., Sydney, Australia). Approximately 5 min before commencement of the measurement, participants were requested to be in a supine position and in a relaxed state. Through palpation, the participant's carotid artery was located to identify the strongest pulse point. The carotid pulse was measured using a tonometer, while the femoral pulse was measured by a femoral cuff placed around the thigh of the participant. The distance between the carotid pulse point and upper femoral cuff was noted, and 80% of the distance was calculated and entered. PWV was thus measured along the descending thoracic abdominal aorta using the foot-to-foot velocity method [32].

Renal function was measured by determining the urinary albumin-to-creatinine ratio using spot urine samples that were obtained early in the morning when participants arrived at the research facility.

Biological sampling and biochemical analysis

Fasting morning blood samples were collected by a registered nurse. Participants were also asked to provide a spot urine sample. All samples were immediately taken to the on-site laboratory. Blood samples were then centrifuged and aliquoted into cryovials for storage in biofreezers at −80 °C until analysis. Serum samples were analyzed using a Cobas Integra® 400 plus (Roche, Basel, Switzerland) to measure total cholesterol (TC), high-density lipoprotein (HDL), low-density lipoprotein (LDL), triglycerides (TG), glucose, C-reactive protein (CRP), and gamma-glutamyl transferase (GGT). Cotinine was analyzed using a chemiluminescence method on an Immulite system (Siemens, Erlangen, Germany). Spot urine samples were analyzed for albumin and creatinine using a Cobas Integra® 400plus (Roche, Basel Switzerland).

Statistical analyses

Statistical analyses were performed using Statistica v13.3 (TIBCO software Inc, Palo Alto, CA, USA), and GraphPad Prism 5.03 (GraphPad Software, San Diego) was used for graphics. All variables were tested for normality using formal tests (Kolmogorov–Smirnov test and Shapiro–Wilk test) as well as graphical methods (histograms). Variables with a non-Gaussian distribution were logarithmically transformed (weight, BMI, WC, LVMi, CIMT, PWV, ACR, TC, LDL, HDL, TG, glucose, CRP, GGT, and cotinine). Normally distributed data are presented as arithmetic mean ± standard deviation, and logarithmically transformed variables are represented by geometric mean and the 5th

and 95th percentile intervals. The total group was also split for ethnicity, and differences between the two ethnic groups were determined by independent t tests, and for categorical data by chi-square tests. We performed Pearson correlations for the associations between all dependent variables (subclinical organ damage measures) and independent variables (all BP measurements) in the total sample and within each ethnic group. We used Williams's t test [33] to determine whether the above mentioned Pearson correlations in the total sample differed significantly ($p < 0.05$). We also determined whether correlations between the black and white groups differed significantly using Fisher's Z transformation.

Results

The baseline characteristics of the total study population are shown in Table 1. The mean age (±SD) of the study population was 24.5 ± 3.11 years, 48% of the study population was male, and 50% of the study population was black. The mean clinic brachial blood pressure was 119/78.6 mmHg. The characteristics of the two ethnic groups in Table 2 show higher bDBP and cSBP in the black population. The 24-h SBP, daytime SBP, and nighttime SBP were all higher in the white population (all $p \le 0.026$). The subclinical organ damage marker CRAE was narrower in the black population ($p < 0.001$), while LVMi, CIMT, PWV, and ACR were comparable between the two ethnic groups (all $p > 0.05$).

In Fig. 1, the correlations between various measures of BP and subclinical organ damage markers in the total group are compared. The results (Fig. 1 and Supplementary Table 1) indicated that CRAE and PWV were associated with all the measures of BP (bSBP, bDBP, cSBP, 24SBP, 24DBP, daySBP, dayDBP, nightSBP, and nightDBP, all $p \le 0.002$). LVMi was also associated with all BP measure except 24DBP and nightDBP. CIMT showed weak correlations and was only associated with bSBP, 24SBP, daySBP, and nightSBP. ACR also showed weak negative correlations with all 24 ambulatory blood pressure measurements. Correlations of BP readings with subclinical organ damage markers that differed ($p < 0.05$) are indicated in Fig. 1 with the same letter (Supplementary Table 2).

CRAE showed a negative association with clinic brachial DBP ($r = -0.30$, $p < 0.001$), which was stronger than the correlations of CRAE with 24SBP, daySBP, dayDBP, nightSBP, and nightDBP.

LVMi was positively associated with clinic bSBP ($r = 0.35$, $p < 0.001$), which was stronger than the correlations of LVMi with bDBP, cSBP, 24DBP, dayDBP, nightSBP, and nightDBP.

Table 1 Baseline characteristics of the study population

Variables	*N*	
Sex, men, *n* (%)	1202	578 (48.1)
Ethnicity black, *n* (%)	1202	606 (50.4)
Age (years)	1202	24.5 ± 3.11
Socio-economic status		
Low, *n* (%)	1202	476 (39.6)
Middle, *n* (%)	1202	347 (28.9)
High, *n* (%)	1202	379 (31.5)
Anthropometric measurements		
Height (m)	1202	168 ± 9.52
Weight (kg)	1202	69.3 (48.9; 103)
Body mass index (kg/m^2)	1202	24.5 (18.0; 35.3)
Waist circumference (cm)	1201	79.2 (64; 103)
Blood pressure (mmHg)		
Clinic		
Brachial SBP	1199	119 ± 11.7
Brachial DBP	1199	78.6 ± 7.66
Central SBP	1201	107 ± 9.51
Ambulatory		
24-h SBP	1188	117 ± 9.45
24-h DBP	1188	68.7 ± 5.87
Day time SBP	1188	122 ± 9.83
Day time DBP	1188	73.4 ± 6.44
Night time SBP	1175	108 ± 10.5
Night time DBP	*1175*	*59.4 ± 6.73*
Measures of subclinical organ damage		
CRAE (MU)	1111	159 (141; 180)
LVMi (g/m^2)	1197	71.6 (49.5; 105)
CIMT (mm)	1198	0.44 ± 0.07
PWV (m/s)	1154	6.29 (5.10; 7.85)
ACR (mg/g)	1200	0.51 (0.16; 2.35)
Biochemical markers		
Total cholesterol (mmol/L)	1196	3.57 (1.99; 5.80)
HDL-c (mmol/L)	1196	1.08 (0.57; 1.89)
LDL-c (mmol/L)	1196	2.25 (1.09; 4.18)
Triglycerides (mmol/L)	1195	0.72 (0.32; 1.82)
Glucose (mmol/L)	1195	3.94 (2.49; 0.55)
CRP (mg/L)	1196	0.88 (0.08; 9.42)
Health behaviours		
GGT (U/L)	1196	18.2 (6; 54.8)
Self-reported alcohol use, *n* (%)	1194	666 (55.8)
Self-reported tobacco use, *n* (%)	1201	286 (23.8)
Cotinine for those >10 ng/mL	302	138 (16.5; 481)

Data are arithmetic mean ± SD or geometric mean (5th and 95th percentile intervals) for logarithmically transformed variables. All blood pressure values are measured in mmHg

bSBP brachial systolic blood pressure, *bDBP* brachial diastolic blood pressure, *cSBP* central systolic blood pressure, *24-h SBP* 24-h systolic blood pressure, *24-h DBP* 24-h diastolic blood pressure, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *CRAE* central retinal arteriolar equivalent, *LVMi* left ventricular mass index, *CIMT* carotid intima media thickness, *PWV* pulse wave velocity, *ACR* albumin-to-creatinine ratio, *HDL-c* high density lipoprotein cholesterol, *LDL-c* low density lipoprotein cholesterol, *CRP* C-reactive protein, *GGT* γ-glutamyl transferase

CIMT was positively correlated with clinic bSBP ($r = 0.10$, $p = 0.001$), which was significantly stronger than the correlations of CIMT with bDBP, dayDBP, and nightDBP.

Table 2 Baseline characteristics of the black and white participants

Variables	Black $N = 606$	White $N = 596$	p values
Sex, men, n (%)	294 (48.5)	284 (47.7)	0.76
Age (years)	24.5 ± 3.17	24.6 ± 3.06	0.55
Socio-economic status			
Low, n (%)	357 (58.9)	119 (20)	<0.001
Middle, n (%)	164 (27.1)	183 (30.7)	<0.001
High, n (%)	85 (14)	294 (49.3)	<0.001
Anthropometric measurements			
Height (m)	168.42 ± 9.52	164.35 ± 8.37	<0.001
Weight (kg)	77.6 (47; 92.4)	81.3 (51.7; 110)	<0.001
Body mass index (kg/m^2)	24.0 (17.6; 35.5)	24.5 (18.9; 35.5)	<0.001
Waist circumference (cm)	77.6 (63.0; 96.9)	81.3 (64.9; 107)	<0.001
Blood pressure (mmHg)			
Clinic			
Brachial SBP	119 ± 11.6	118 ± 11.7	0.052
Brachial DBP	79.7 ± 7.95	77.5 ± 7.19	<0.001
Central SBP	109 ± 9.18	105 ± 9.37	<0.001
Ambulatory			
24-h SBP	116 ± 8.98	118 ± 9.81	<0.001
24-h DBP	68.8 ± 5.92	68.6 ± 5.85	0.47
Day-time SBP	120 ± 9.25	123 ± 10.2	<0.001
Day-time DBP	73.4 ± 6.40	73.4 ± 6.50	0.96
Night-time SBP	107 ± 10.0	109 ± 10.9	0.026
Night-time DBP	59.7 ± 6.77	59.1 ± 6.69	0.13
Measures of subclinical organ damage			
CRAE (MU)	159 (139; 177)	162 (142; 181)	<0.001
LVMi (g/m^2)	72.4 (48.5; 110)	70.8 (50.2; 103)	0.94
CIMT (mm)	0.44 ± 0.07	0.43 ± 0.07	0.31
PWV (m/s)	6.31 (5.10; 7.96)	6.17 (5.10; 7.70)	0.089
ACR (mg/g)	0.51 (0.15; 2.44)	0.49 (0.17; 2.34)	0.28
Biochemical markers			
Total cholesterol (mmol/L)	3.31 (1.94; 5.10)	3.80 (2.11; 6.10)	<0.001
HDL-c (mmol/L)	2.09 (0.57; 1.83)	2.14 (0.56; 2.02)	0.53
LDL-c (mmol/L)	3.09 (0.99; 3.71)	3.55 (1.20; 4.42)	<0.001
Triglycerides (mmol/L)	1.70 (0.31; 1.37)	1.86 (0.33; 2.10)	<0.001
Glucose (mmol/L)	3.80 (2.33; 5.44)	4.07 (2.60; 5.58)	<0.001
CRP (mg/L)	2.58 (0.09; 10.9)	2.19 (0.08; 8.08)	0.001
Health behaviours			
GGT (U/L)	21.9 (8.42; 66.2)	14.8 (5.40; 47.2)	<0.001
Self-reported alcohol use, n (%)	334 (55.1)	332 (55.7)	0.99
Self-reported tobacco use, n (%)	154 (25.4)	132 (22.2)	0.18
Cotinine for those >10 ng/mL	151 (18.9; 499)	123 (15.3; 461)	0.10

Data are arithmetic mean ± SD or geometric mean (5th and 95th percentile intervals) for logarithmically transformed variables. All blood pressure values are measured in mmHg

bSBP, brachial systolic blood pressure, *bDBP* brachial diastolic blood pressure, *cSBP* central systolic blood pressure, *24-h SBP* 24-h systolic blood pressure, *24-h DBP* 24-h diastolic blood pressure, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *CRAE* central retinal arteriolar equivalent, *LVMi* left ventricular mass index, *CIMT* carotid intima media thickness, *PWV* pulse wave velocity, *ACR* albumin-to-creatinine ratio, *HDL-c* high density lipoprotein cholesterol, *LDL-c* low density lipoprotein cholesterol, *CRP* C-reactive protein, *GGT* γ-glutamyl transferase

PWV was positively correlated with clinic bDBP ($r = 0.49$, $p < 0.001$), which was stronger than the positive correlations of PWV with bSBP, cSBP, 24SBP, 24DBP, daySBP, dayDBP, nightSBP, and nightDBP.

ACR showed negative associations with 24SBP ($r = -0.09$, $p = 0.002$) and daySBP ($r = -0.09$, $p = 0.002$), which were stronger than the correlations of ACR with bSBP, bDBP, and cSBP.

Sensitivity analysis

To determine the possible confounding effect of other cardiovascular risk factors on the association between markers of subclinical organ damage and measures of BP, a multivariate linear regression analysis was performed (Table 3). The covariates included in all models were age, sex, ethnicity, SES, BMI, and cotinine. All of the previous associations between the dependent variables (subclinical organ damage measures) and independent variables (all BP measurements) remained significant (all $p < 0.035$).

When reviewing the comparisons of correlations performed within each ethnic group (Fig. 2, Supplementary Tables 3 and 4), we found correlations in both populations for CRAE and PWV with all BP measures (all $p < 0.001$). There were no ethnic differences in the strength of correlations between CRAE and BP measures.

The white population showed a stronger correlation of LVMi with 24SBP ($r = 0.34$, $p < 0.001$) than the black population.

CIMT correlations were weak and nonsignificant overall. In the black population, clinic bDBP showed a stronger positive correlation ($r = 0.09$, $p = 0.025$) than in the white population.

PWV in the white population showed stronger positive correlations with 24SBP ($r = 0.36$, $p < 0.001$), daySBP ($r = 0.37$, $p < 0.001$), and nightSBP ($r = 0.27$, $p < 0.001$) than in the black population.

ACR in the white population showed stronger negative correlations with bSBP ($r = -0.12$, $p = 0.004$), cSBP ($r = -0.11$, $p = 0.008$), 24SBP ($r = -0.18$, $p < 0.001$), 24DBP ($r = -0.14$, $p = 0.001$), daySBP ($r = -0.18$, $p < 0.001$), dayDBP ($r = -0.14$, $p = 0.001$), and nightSBP ($r = -0.14$, $p = 0.001$) than in the black population.

Discussion

We compared the strength of associations of BP measured in the clinic (brachial and central blood pressure) and 24-h ambulatory blood pressure with measures of subclinical target organ damage in young adults. Overall, we found that arteriolar narrowing, LVMi, and arterial stiffness had the strongest associations with BP. A prominent finding was that, against expectations, clinic brachial blood pressure had stronger associations with arteriolar narrowing, LVMi, and arterial stiffness than 24-h ambulatory and central blood pressure. Furthermore, carotid wall thickness and albumin-

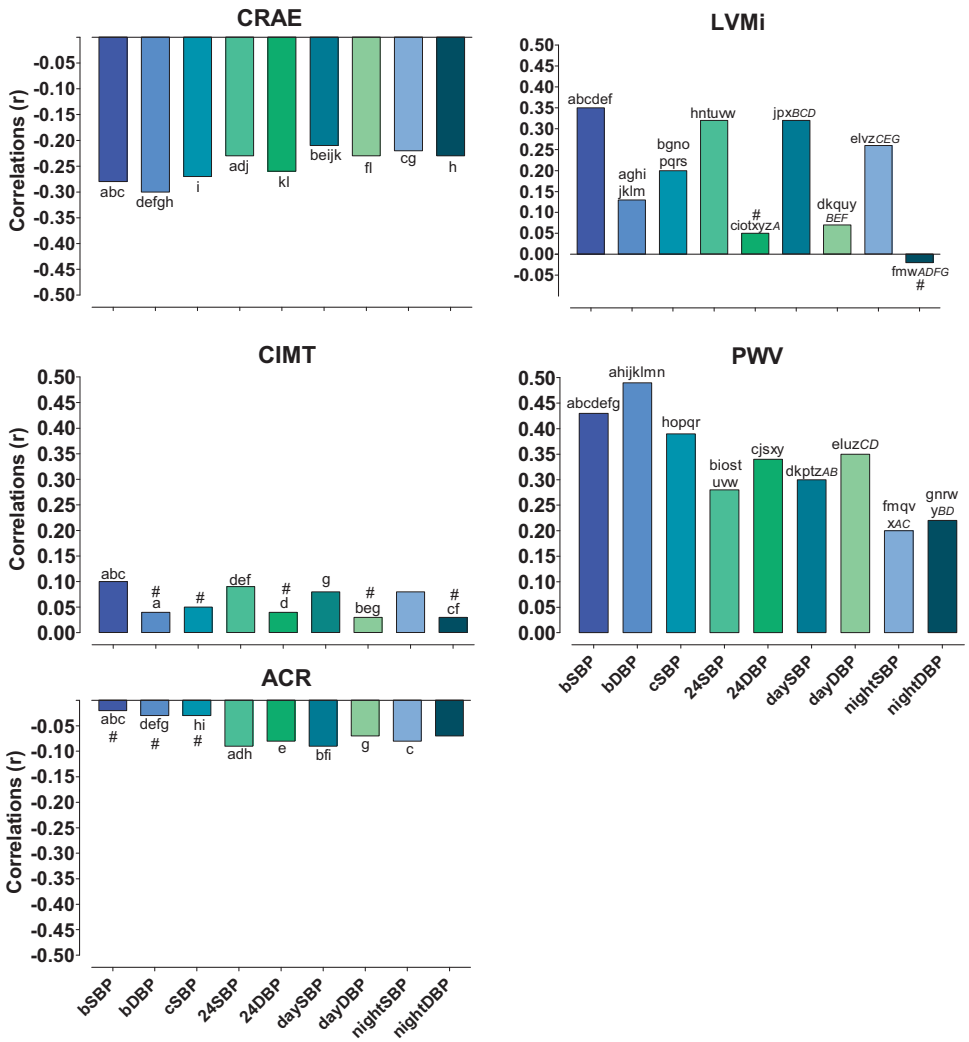

Fig. 1 Comparing the strength of correlations between different subclinical organ damage markers and various measures of blood pressure in the total population. Bars with the same letter differ significantly, $p < 0.05$. #Weak correlation with $p > 0.05$. *bSBP* brachial systolic blood pressure, *bDBP* brachial diastolic blood pressure, *cSBP* central systolic blood pressure, *24-h SBP* 24-h systolic blood pressure, *24-h DBP* 24-h diastolic blood pressure, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *CRAE* central retinal arteriolar equivalent, *LVMi* left ventricular mass index, *CIMT* carotid intima media thickness, *PWV* pulse wave velocity, *ACR* albumin-to-creatinine ratio

to-creatinine ratio showed weak associations with all BP readings.

The secondary aim was to compare whether differences exist between black and white adults when comparing associations between various blood pressures and markers of subclinical target organ damage. No differences were found between the black and white groups in the strength of correlations of arteriolar narrowing, LVMi, and cIMT with the various blood pressures. Marked differences were observed between the ethnic groups for correlations between arterial stiffness and 24-h SBP, daytime SBP, and nighttime SBP, with the correlations being stronger in the white group. Furthermore, it is notable that the albumin-to-creatinine ratio in all cases showed weak negative associations with BP in the white group, where all correlations in the black group were nonsignificant.

In comparison with previous studies, a large cohort study of 66,636 participants aged 58.4 years found 24-h ambulatory blood pressure to be a better predictor of cardiovascular mortality than clinic brachial blood pressure [18]. A longitudinal epidemiological trial of 1599 participants with a mean age of 71.4 years compared the associations between central and clinic brachial blood pressure and markers of target organ damage, including left ventricular hypertrophy, left ventricular dysfunction, carotid plaque, arterial stiffness, and microalbuminuria [34]. They found central blood pressure to be better associated with these target organ damage markers [34]. This is in contrast to our study, as we found that clinic brachial blood pressure was associated more strongly with subclinical target organ damage measures in young adults than either 24-h ambulatory or central blood pressure.

Evidence indicating which BP reading is more predictive of subclinical target organ damage is limited, particularly in young populations. One study also performed in South Africans reported that clinic brachial blood pressure and 24-h ambulatory blood pressure were similarly associated with target organ damage. This study included 458 randomly selected participants with a mean age of 43 years [35].

Table 3 Multiple regression analyses between markers of subclinical organ damage and measures of blood pressure

	CRAE (MU)		LVMi (g/m^2)		cIMT (mm)		PWV (m/s)		ACR (mg/g)	
	Adjusted R^2	Std β (95% CI)	Adjusted R^2	Std β (95% CI)	Adjusted R^2	Std β (95% CI)	Adjusted R^2	Std β (95% CI)	Adjusted R^2	Std β (95% CI)
Clinic										
bSBP (mmHg)	**0.095**	**−0.298 (−0.368; −0.228)**	**0.256**	**0.128 (0.067; 0.189)**	**0.027**	**0.121 (0.052; 0.191)**	**0.314**	**0.345 (0.286; 0.405)**	**0.031**	**0.097 (0.028; 0.166)**
bDBP (mmHg)	**0.106**	**−0.263 (−0.324; −0.202)**	0.245	0.007 (−0.047; 0.061)	0.017	0.013 (−0.048; 0.074)	**0.379**	**0.408 (0.358; 0.458)**	0.032	0.033 (−0.028; 0.094)
Central SBP (mmHg)	**0.089**	**−0.221 (−0.286; −0.156)**	**0.249**	**0.077 (0.020; 0.133)**	0.019	0.054 (−0.011; 0.119)	**0.327**	**0.344 (0.289; 0.398)**	0.032	0.044 (−0.020; 0.108)
Ambulatory										
24-h SBP (mmHg)	**0.111**	**−0.276 (−0.352; −0.199)**	**0.252**	**0.121 (0.047; 0.180)**	**0.036**	**0.173 (0.090; 0.241)**	**0.255**	**0.187 (0.120; 0.254)**	0.031	0.038 (−0.036; 0.115)
24-h DBP (mmHg)	**0.111**	**−0.251 (−0.313; −0.189)**	0.245	−0.042 (−0.099; 0.009)	0.020	0.040 (−0.025; 0.099)	**0.303**	**0.281 (0.228; 0.334)**	0.031	−0.0119 (−0.080; 0.043)
Day SBP (mmHg)	**0.086**	**−0.244 (−0.320; −0.168)**	**0.253**	**0.129 (0.056; 0.187)**	**0.031**	**0.145 (0.063; 0.212)**	**0.261**	**0.210 (0.144; 0.276)**	0.031	0.035 (−0.038; 0.111)
Day DBP (mmHg)	**0.092**	**−0.215 (−0.276; −0.153)**	0.244	−0.017 (−0.073; 0.034)	0.019	0.020 (−0.044; 0.079)	**0.304**	**0.282 (0.228; 0.333)**	0.030	−0.017 (−0.078; 0.044)
Night SBP (mmHg)	**0.085**	**−0.223 (−0.294; −0.152)**	**0.246**	**0.066 (−0.002; 0.122)**	**0.246**	**0.066 (0.061; 0.201)**	**0.240**	**0.093 (0.031; 0.156)**	**0.246**	**0.066 (−0.050; 0.090)**
Night DBP (mmHg)	**0.089**	**−0.203 (−0.264; −0.143)**	**0.249**	**−0.079 (−0.134; −0.029)**	0.249	−0.079 (−0.029; 0.092)	**0.268**	**0.190 (0.138; 0.243)**	**0.249**	**−0.079 (−0.089; 0.030)**

Variables included in the models were age, sex, ethnicity, socioeconomic status, body mass index, and cotinine.

CRAE central retinal arteriolar calibre, *LVMi* left ventricular mass index, *cIMT* carotid intima media thickness, *PWV* pulse wave velocity, *ACR* albumin-to-creatinine ratio, *SBP* systolic blood pressure, *DBP* diastolic blood pressure

Bold text denotes statistical significance ($p < 0.05$)

Our findings of stronger correlations between clinic brachial BP and target organ damage are difficult to explain. A notable difference between our population and those from previous studies is the relatively young age (mean age of 24.5 years vs. mean ages of 58.4 and 71.4 years) [18, 34]. Our study population therefore presents with early subclinical target organ changes, as our eligibility criteria required participants to be apparently healthy and free from any chronic disease. A possible explanation for our findings might lie in the physiological difference between clinic and ambulatory blood pressure. Ambulatory blood pressure has the ability to detect BP variations outside of the clinic and hence the ability to diagnose masked hypertension, white coat hypertension, and nocturnal hypertension [36]. The anxiety accounting for the white coat effect during clinic blood pressure measurement may result in higher clinic blood pressure—the exact reason why ambulatory blood pressure measurements are recommended as the gold standard test [36]. This higher clinic blood pressure is potentially due to sympathetic activation when measuring clinic brachial blood pressure [37]. Whether the office BP measurements in our study are a better representation of increased cardiovascular risk due to indirectly capturing a measure of sympathetic activation needs to be further explored.

An important observation in our young population is that overall BP is associated more strongly with arterial stiffness, arteriolar narrowing, and LVMi, whereas cIMT and albumin-to-creatinine ratio are associated only weakly with BP. Other studies corroborated our findings, where studies in children also found increased BP to be linked with retinal arteriolar narrowing, LVMi, and arterial stiffness [38, 39]. The LVMi reflects small changes in ventricular mass and may be due to cardiac remodeling. Over time, this can progress to left ventricular hypertrophy [40]. This cardiac remodeling may be due to small increases in BP within this young healthy population even when BP is still within a normal range. A further result of increasing BP is remodeling, which occurs within the vasculature, resulting in narrowing of the arterioles as measured within the retina [40]. Because increased cIMT and albuminuria are anticipated to take years to develop into atherosclerosis and renal dysfunction [41], this may explain why no associations with BP were found at this young age.

To our knowledge, it has not yet been determined whether specific measures of BP is more strongly associated with target organ damage in black populations than in white populations. Overall, we found similar associations between BP and target organ damage in the black and white groups. We did, however, show that 24-h nighttime and daytime blood pressures correlated more strongly with arterial stiffness in the white population.

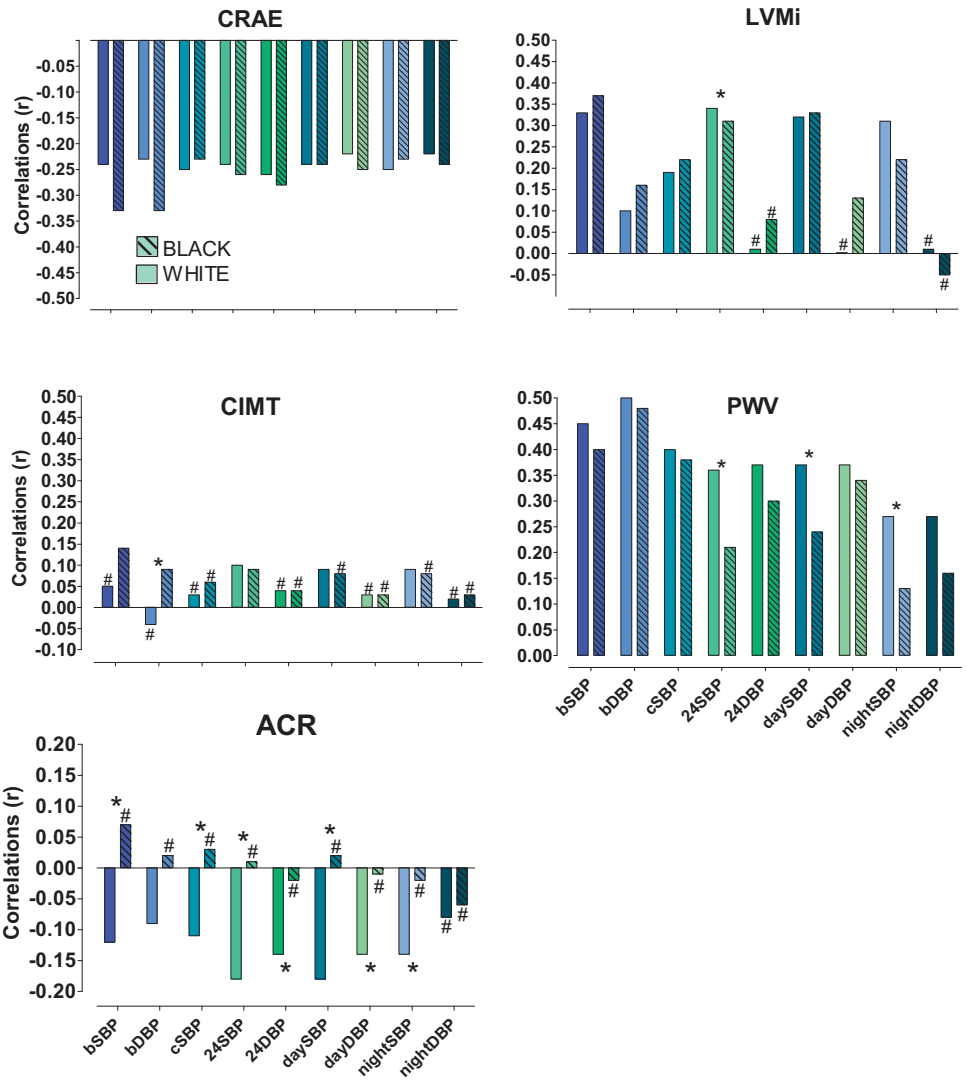

Fig. 2 Comparing the strength of correlations between black and white groups regarding the associations between subclinical organ damage and various measures of blood pressure. #Nonsignificant correlations, $p > 0.05$. *Significant difference between correlations of black and white groups, $p < 0.05$. *bSBP* brachial systolic blood pressure, *bDBP* brachial diastolic blood pressure, *cSBP* central systolic blood pressure, *24-h SBP* 24-h systolic blood pressure, *24-h DBP* 24-h diastolic blood pressure *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *CRAE* central retinal arteriolar equivalent, *LVMi* left ventricular mass index, *CIMT* carotid intima media thickness, *PWV* pulse wave velocity, *ACR* albumin-to-creatinine ratio

In young white adults we found weak negative associations between BP and the urinary albumin-to-creatinine ratio, with weak nonsignificant associations in the black population. The reason for the negative correlations between BP and the albumin-to-creatinine ratio in the white cohort is unclear, as it is unlikely that glomerular and vascular endothelial dysfunction will be present at this young age. In a healthy young cohort, only small amounts of albumin were present within the urine because most of the albumin filtered by the glomeruli was reabsorbed by the renal tubules [42]. In older populations [43], it is generally observed that reabsorption of filtered albumin is overwhelmed when the load is too large due to the presence of glomerular and vascular endothelial dysfunction.

The strengths and limitations of the study should be taken into consideration when interpreting our findings. Our study did not include longitudinal data, which may have improved our understanding regarding early changes in BP and related target organ damage. This study included data from young black adults, thereby contributing to an area where limited data on early cardiovascular disease development are available.

In conclusion, contrary to expectations, we found in a large sample of young adults that overall clinic brachial blood pressure correlated more strongly with measures of early target organ damage than central and ambulatory blood pressure. No distinct differences were observed between correlations of BP and measures of target organ damage in the black and white populations.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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