Monocyte Chemoattractant Protein-1 and Large Artery Structure and Function in Young Individuals: The African-PREDICT Study

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To better understand hypertension development, the authors determined whether monocyte chemoattractant protein-1 (MCP-1) is associated with arterial stiffness (pulse wave velocity [PWV]) and carotid intima-media wall thickness (cIMT) in a young apparently healthy black and white population (N=403, aged 20–30 years). Carotid-femoral PWV, central systolic blood pressure, and cIMT were measured, and MCP-1, reactive oxygen species, inflammatory markers (interleukin 6, tumor necrosis factor α), and endothelial activation (intercellular adhesion molecule, vascular cell adhesion molecule) were determined from blood samples. Although carotid-femoral PWV and cIMT were similar between blacks and whites, black men and women showed higher central systolic blood pressure, MCP-1, and reactive oxygen species than whites (all $P<.05$). In addition, black women had higher brachial blood pressure and interleukin 6 (all $P<.001$). A consistent positive association only in black women between cIMT and MCP-1 in multiple regression analyses was found ($R^2=0.151$, $\beta=0.248$; $P=.021$). In this model, cIMT was also independently associated with vascular cell adhesion molecule ($\beta=0.251$; $P=.022$). The authors found elevated central systolic blood pressure and MCP-1 in young blacks, where cIMT was independently associated with MCP-1 in black women. *J Clin Hypertens (Greenwich).* 2017;19:67–74. © 2016 Wiley Periodicals, Inc.

Hypertension and cardiovascular disease (CVD) have reached epidemic proportions in sub-Saharan Africa,[1,2] and as with the black population in the United States,[3] the South African black population shows a high prevalence of hypertension and an increased risk of developing CVD.[4,5] This elevated cardiovascular risk can, however, only partly be explained by traditional risk factors such as lifestyle, diabetes mellitus, and smoking.[4,6] Large artery stiffness is recognized as an independent predictor of CVD morbidity and mortality.[7,8] The black population presents with impaired vascular and endothelial function, accompanied by greater arterial stiffness when compared with whites.[9] Increased carotid intima-media thickness (cIMT) and stiffness has also been demonstrated in African Americans.[10,11]

When viewing endothelial dysfunction in black populations, evidence indicates that increased blood pressure (BP) is characterized by elevated plasma levels of inflammatory markers, adhesion molecules, and chemokines when compared with whites.[12–14]

Biomarkers and their association with arterial stiffness and atherosclerosis have increasingly been the subject of efforts to make risk stratification and early detection of CVD more efficient.[15,16] Monocyte chemoattractant protein-1 (MCP-1) is an extensively investigated chemokine with regard to its relationship with increased risk for hypertension and CVD.[17–19] MCP-1 is produced by endothelial cells and vascular smooth muscle cells, among other cellular sources, in response to various stimuli.[20] Interleukin (IL) 1, IL-4, IL-6, and tumor necrosis factor α (TNF-α), among other factors, stimulate the expression of MCP-1 by vascular endothelial cells.[21] MCP-1 binds only to the CCR2 receptor, which is constantly expressed on monocytes.[22] MCP-1 is therefore a chemoattractant for human monocytes, and alone or in combination with other cytokines attract monocytes to its site of release, and cause cellular activation of specific immunological functions related to immune defense.[20] Apart from hypertension, elevated MCP-1 and its receptor CCR2 are therefore also involved in the development of atherosclerosis[23] and are associated with increased risk of myocardial infarction,[23] coronary angioplasty,[24] and stent restenosis.[25]

Literature on MCP-1 in black populations is scant and to our knowledge no studies have reported MCP-1 levels in a healthy young black population to evaluate its potential usefulness as an early indicator of carotid wall thickness or large artery stiffness. We therefore investigated the association of cIMT and large artery stiffness with MCP-1 in a young and apparently healthy black and white population.

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METHODS

Study Design

This substudy forms part of the larger African Prospective Study on the Early Detection and Identification of Cardiovascular Disease and Hypertension (African-

PREDICT). The central aim of the longitudinal African-PREDICT study is to understand the early pathological changes in young individuals as part of hypertension development. The study is presently in its baseline phase with the aim to include a total of 1200 participants. Participant recruitment takes place in the Potchefstroom and surrounding areas in South Africa, using recruitment methods such as active contact via field workers, access through the workplace, and advertisements placed in local newspapers and radio stations. The participants therefore represent an availability sample and are stratified into different ethnic groups (black and white), sex, and socioeconomic class groups (low, mid, and high).

Inclusion criteria were apparently healthy black and white men and women aged 20 to 30 years with systolic BP (SBP) <140 mm Hg/<90 mm Hg and no known CVD, not taking any BP medication, no chronic disease, and not pregnant or breastfeeding. Participants gave written informed consent after the procedures of the study were explained to all volunteers. The Health Research Ethics Committee of the North-West University approved the study (NWU-00001-12-A1).

In this cross-sectional substudy we included the first 403 participants who were enrolled into the study during the period from February 2013 to September 2014, consisting of black (n=198) and white (n=205) men and women.

Questionnaires

Demographic and lifestyle questionnaires and the global physical activity questionnaire (GPAQ)[26] were used to assess alcohol use, smoking habits, and physical activity level.

Anthropometric Measurements

Anthropometric measurements were performed according to standard methods described by Marfell-Jones and colleagues[27] and included height (SECA 213 Portable Stadiometer, Hamburg, Germany), weight (SECA 813 Electronic Scale, Hamburg, Germany), and waist circumference (WC) (Lufkin Steel Anthropometric Tape, Apex Tool Group, Glencoe, MD).

Cardiovascular Measurements

Duplicate office brachial BP measurements were conducted on the left and right arms with a 5-minute interval while the participants were seated and in a rested state using the Dinamap Procare 200 BP Monitor (GE Medical Systems, Milwaukee, WI. Participants were also fitted with a 24-hour ambulatory BP monitoring (ABPM) device (CardioXplore CE120, Meditech, Budapest, Hungary) validated by the British Hypertension Society and Association for the Advancement of Medical Instrumentation.

Arterial stiffness was assessed according to the manufacturer's instructions to determine carotid-femoral pulse wave velocity (cfPWV) using the validated SphygmoCor XCEL device (AtCor Medical Pty Ltd., Sydney, Australia).[23,24] cfPWV was measured along the descending thoracic-abdominal aorta using the foot-to-foot velocity method. Measurements were taken in duplicate, and the mean value was reported. The Sphygmocor XCEL has strict built-in quality-control parameters to ensure a valid, reproducible waveform. Any pulse wave measurements not considered of sufficient quality were repeated. These were based on an operator index (composite quality-control parameter) and additional quality indices (reflecting the degree of variation outside of acceptable limits).[28]

B-mode ultrasonography was used to determine the cIMT of the left and right common carotid artery (General Electric Vivid E9, GE Vingmed Ultrasound A/S, Horten, Norway). The images were digitized and imported into the Artery Measurement Systems Software for dedicated analyses (Tomas Gustavsson, Sweden). All ultrasound cIMT images were taken and analyzed by an experienced single observer. The mean cIMT values of the images were reported.

Biochemical Analyses

Participants were required to fast for at least 8 hours. A registered nurse took a blood sample from the antebrachial vein using a winged infusion set. An early-morning spot urine sample was taken. All samples were immediately taken to the on-site laboratory and appropriately allocated into cryovials and stored in biofreezers at −80°C until analyses. Basic serum analyses included total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), triglycerides (TGs), glucose, high-sensitivity C-reactive protein (hsCRP), creatinine, gamma-glutamyl transferase (GGT), albumin, and urea (Cobas Integra 400plus, Roche, Basel, Switzerland). Total serum peroxides were determined with a high-throughput spectrophotometric kinetic assay as an indicator of reactive oxygen species (ROS). The assay measures the generic peroxide-induced modification of the chromogen *N*, *N*-dimethyl-*para*-phenylendiamine expressed as units (1 unit equaling 1 mg H_2O_2/L).[29] Cotinine was analyzed using the chemiluminescent method on the Immulite nicotine metabolite assay (Siemens, Erlangen, Germany), and MCP-1 with a Quantikine Human CCL2/MCP-1 immunoassay (R&D Systems, Inc., Minneapolis, MN; detectable range 72–295 ng/mL). This assay uses the quantitative sandwich enzyme immunoassay technique. Furthermore, serum intercellular adhesion molecule (ICAM; detectable range 100–307 ng/mL), vascular cell adhesion molecule (VCAM; detectable range 341–897 ng/mL), IL-6 (detectable range 0.435–9.57 pg/mL), and tumor necrosis factor-α (detectable range ND-2.139 pg/mL) were measured using Quantikine ELISA kits (R&D Systems, Inc.).

Statistical Analyses

For database management and statistical analyses, we used Statistica software version 12 (Statsoft Inc., Tulsa, Oklahoma, USA). We tested for the interaction of

ethnicity and sex regarding the associations of cfPWV and cIMT with MCP-1. Means and proportions were compared between blacks and whites using independent *t* tests and chi-square tests, respectively. The biochemical variables with a skewed distribution (MCP-1, TNF-α, hsCRP, IL-6, ROS, total cholesterol, triglycerides, and GGT) were normalized with natural logarithmic transformation. Continuous data were presented as arithmetic means±standard deviations or geometric means (5th and 95th percentile intervals) for logarithmically transformed variables. We determined ethnicity- and sex-specific Pearson and partial correlation coefficients between cardiovascular measurements (cfPWV and cIMT) and MCP-1, with adjustment for age and mean arterial pressure. Multiple regression analyses were performed with either cfPWV or cIMT as dependent variables and MCP-1 as the main independent variable. Independent variables included in the model were age, mean arterial pressure, LDL-C, waist circumference, glucose, TNF-α, VCAM-1, and ROS. Other covariates considered for entry in the models were IL-6, hsCRP, ICAM-1, HDL-C, central SBP, 24-hour BP, and body mass index (BMI). A $P<.05$ was regarded as statistically significant.

RESULTS

We found a significant interaction with sex for the association of cfPWV and MCP-1 ($P=.042$), and a significant interaction with ethnicity for the association of cIMT and MCP-1 ($P=.007$). Based on these interactions, as well as our research aim and previous studies confirming differential development of hypertension in black and white ethnicities,[1,30] we compared the ethnic and sex groups in subsequent analyses.

The characteristics of the study population and measurements are presented in Table I. While the study population included young adults aged 20 to 30 years, the mean ages of white men ($P=.014$) and women ($P=.015$) were older than their black counterparts. Black men had lower indices of obesity (BMI $P=.001$ and WC $P=.001$) and total cholesterol ($P<.001$) than white men, but showed higher values of central SBP ($P=.006$), MCP-1 ($P<.001$), and ROS ($P=.035$). cfPWV and cIMT were similar between black and white men.

Black women had higher indices of obesity (BMI $P=.008$ and WC $P=.031$) but lower total cholesterol levels ($P<.001$) than white women. Similar to the men, black women had higher values of central SBP ($P<.001$), MCP-1 ($P<.001$), and ROS ($P=.003$) than white women, and cfPWV and cIMT were similar between black and white women. In addition, black women also had elevated IL-6 ($P<.001$) but lower markers of endothelial activation (VCAM $P=.005$ and ICAM $P=.002$). Despite similar 24-hour BP, black women had higher office brachial SBP and DBP (both $P<.001$) values and mean arterial BP ($P=.001$) when compared with white women.

In single and partial regression analyses (Table II) and multiple regression analyses (Table III), we found a consistent positive association between cIMT and MCP-1 in black women ($R^2=0.151$; $\beta=0.248$ [0.14–0.35]; $P=.021$). However, we found no significant associations of cfPWV or cIMT with MCP-1 in any of the other groups. In addition to the independent association between cIMT and MCP-1 in black women (Table III), cIMT was also positively associated with VCAM-1 ($R^2=0.151$; $\beta=0.251$ [0.14–0.36]; $P=.022$) only in black women and independently of MCP-1. Although the participants were relatively young, a there was a positive association between cfPWV and age in black men ($R^2=0.161$; $\beta=0.250$ [0.13–0.37]; $P=.039$) and women ($R^2=0.184$; $\beta=0.396$ [0.28–0.51]; $P=.001$) but not in white men ($R^2=0.308$; $\beta=0.51$ [0.02–0.24]; $P=.24$) and women ($R^2=0.059$; $\beta=0.171$ [0.08–0.27]; $P=.078$).

Sensitivity Analyses

We have previously shown that despite screening participants for normotensive office BPs, 16% of this cohort presented with masked hypertension.[31] To confirm whether our finding is robust after exclusion of participants with masked hypertension, we repeated our multiple regression analyses in black women for the association between cIMT and MCP-1, as well as VCAM-1. Upon doing so, our findings remained unchanged for MCP-1 ($R^2=0.161$; $\beta=0.27$; $P=.027$) and VCAM-1 ($\beta=0.26$; $P=.036$).

DISCUSSION

To evaluate the potential usefulness of MCP-1 as an early biomarker of CVD development in young healthy black and white adults, we investigated the association of carotid wall thickness and arterial stiffness with MCP-1 in a young bi-ethnic population. We found that the cardiovascular profiles of black men and women seemed more vulnerable due to elevated MCP-1 and central SBP compared with their white counterparts. Although large artery stiffness (cfPWV) was similar between the black and white groups, it was positively associated with age in the black population only, which may support the notion of early vascular aging in young black adults.[32,33] Our main finding was that carotid wall thickness was positively associated with MCP-1 in black women but in none of the other groups. In the black women, the link between cIMT and MCP-1 was supported by a consistent association between cIMT and the endothelial activation marker VCAM-1.

It is important to view this finding while taking into account the overall cardiovascular profile of our young black group. We found that although all participants were screened for normal office brachial BP, central SBP was higher in the black men and women compared with the white men and women. Central SBP provides us with a better measurement of the load on central and carotid arteries, and may therefore be a better indicator of vascular damage[34] and cardiovascular outcome.[34,35] Despite our finding of an increased central SBP in blacks, their cfPWV and cIMT values were similar to that of the white group. Apart from central SBP, we

TABLE I. Characteristics of Participants (n=403)

	Black Men (n=91)	White Men (n=80)	*P* Value	Black Women (n=107)	White Women (n=125)	*P* Value
Age, y	24.5±3.01	25.6±2.90	.014	24.5±3.41	25.5±2.85	.015
Anthropometric variables						
Body mass index, kg/m^2	21.9±3.40	28.0±5.64	.001	26.6±5.81	24.6±5.42	.008
Waist circumference, cm	74.5±8.81	91.5±14.1	.001	79.6±11.9	76.1±12.6	.031
Cardiovascular variables						
bSBP, mm Hg	125.8±11.6	124.9±8.42	.59	116.4±10.4	109.7±10.4	<.001
bDBP, mm Hg	82.5±8.82	79.9±6.67	.044	79.1±7.60	74.4±7.27	<.001
bMAP, mm Hg	96.9±9.13	95.0±6.50	.12	91.5±7.95	86.2±7.89	.001
24-H SBP, mm Hg	121.1±9.12	124.3±6.73	.011	118.1±8.64	117.9±8.79	.87
24-H DBP, mm Hg	71.7±6.90	70.7±6.12	.98	69±5.66	68.2±5.71	.93
cSBP, mm Hg	114.6±10.2	110.5±8.55	.006	108.6±8.09	103.4±8.75	<.001
cPP, mm Hg	36.1±5.40	37.7±5.58	.066	31.8±5.17	32.5±4.21	.24
bPP, mm Hg	43.3±7.71	44.9±7.09	.16	37.9±7.25	35.3±6.43	.027
cfPWV, ms^{-1}[a]	6.85±0.74	6.73±0.75	.34	6.04±0.78	6.09±0.78	.54
cIMT, mm[a]	0.48±0.05	0.48±0.05	.81	0.45±0.04	0.46±0.04	.09
Biochemical variables						
Total cholesterol, mmol/L	3.89 (3.70;4.07)	4.73 (4.49;4.98)	<.001	3.83 (3.67;3.99)	4.73 (4.56;4.90)	<.001
HDL-C, mmol/L	1.34±0.35	1.12±0.26	<.001	1.21±0.32	1.61±0.40	<.001
LDL-C, mmol/L	2.36±0.83	3.30±1.04	<.001	2.50±0.81	2.90±0.83	.001
Triglycerides, mmol/L	0.94 (0.82;1.06)	1.21 (1.07;1.34)	.001	0.77 (0.71;0.82)	1.03 (0.91;1.14)	<.001
ROS, units	155.7±45.91	139.6±40.70	.035	228.2±70.63	206.2±101.4	.003
hs-CRP, mg/L	1.61 (0.79;2.44)	2.36 (1.20;3.52)	.091	3.84 (2.96;4.72)	3.18 (2.12;4.25)	.001
MCP-1, pg/mL	190 (181;200)	154 (145;163)	<.001	169 (160;178)	136 (127;145)	<.001
Interleukin 6, pg/mL	1.02 (0.78;1.27)	0.98 (0.78;1.17)	.85	1.45 (1.20;1.70)	0.95 (0.76;1.15)	<.001
TNF-α, pg/mL	1.86 (1.63;2.10)	1.91 (1.80;2.03)	.071	1.94 (1.58;2.29)	1.81 (1.67;1.95)	.57
sICAM-1, ng/mL	140.0±72.84	187.0±62.9	<.001	152.03±82.32	181.0±56.7	.002
sVCAM-1, ng/mL	543.96±124.27	552.07±146.53	.70	536.73±143.15	599.15±185.13	.005
Serum creatinine, umol/L	73.7±13.2	88.2±11.3	<.001	58.1±10.2	66.9±9.89	<.001
Serum albumin, g/L	46.9±3.92	48.8±2.87	<.001	44.7±3.79	46.2±3.10	.003
Urea, mmol/L	3.94±1.10	5.29±1.13	<.001	3.35±0.95	4.38±1.21	<.001
GGT, U/L	38.0±38.3	30.3±27.2	.14	28.10±22.86	16.6±12.7	.001
Cotinine, ng/mL	1.14±1.16	0.63±0.97	.002	0.36±0.73	0.31±0.68	.85
Self-reported lifestyle variables						
Regular physical activity, No. (%)	45/91 (49.5)	33/80 (41.3)	.56	32/107 (29.9)	48/125 (38.4)	.326
Current smoking, No. (%)	51/91 (56.0)	19/80 (23.8)	.001	12/107 (11.2)	13/125 (10.4)	.84
Current drinking, No. (%)	68/91 (74.7)	58/80 (72.5)	.74	55/107 (51.4)	78/125 (62.4)	.091

Abbreviations: bDBP, brachial diastolic blood pressure; bMAP, brachial mean arterial pressure; bPP, brachial pulse pressure; bSBP, brachial systolic blood pressure; cfPWV, carotid-femoral pulse wave velocity; cIMT, carotid intima media thickness; cPP, central pulse pressure; GGT, gamma-glutamyl tranferase; HDL-C, high-density lipoprotein cholesterol; hs-CRP, high-sensitivity C-reactive protein; ICAM-1, intercellular adhesion molecule-1; LDL-C, low-density lipoprotein cholesterol; MCP-1, monocyte chemoattractant protein-1; ROS, reactive oxygen species; TNF-α, tumor necrosis factor-α; VCAM-1, vascular cell adhesion molecule-1. Data are expressed as arithmetic mean±standard deviation or geometric mean with 95% percentile intervals, for logarithmically transformed data, or number (percentage).

[a]Adjusted for mean arterial pressure.

TABLE II. Pearson and Partial Correlations of cfPWV and cIMT With MCP-1

	cfPWV	cIMT
Black men	r=0.11; P=.29	r=0.14; P=.20
White men	r=0.16; P=.18	r=−0.17; P=.14
Black women	r=−0.15; P=.14	r=0.22; P=.02
White women	r=0.03; P=.72	r=0.007; P=.93
Adjusted for age and mean arterial pressure		
Black men	r=0.03; P=.77	r=0.12; P=.28
White men	r=0.09; P=.44	r=−0.13; P=.31
Black women	r=−0.17; P=.10	r=0.31; P=.002
White women	r=−0.03; P=.76	r=−0.03; P=.77

Abbreviations: cfPWV, carotid-femoral pulse wave velocity; cIMT, carotid intima media thickness; MCP-1, monocyte chemoattractant protein-1.

have also previously shown that in this particular study population 16% presented with masked hypertension, with a similar prevalence in black and white participants.[31] Despite their young age, patients with masked hypertension presented with increased cardiovascular risk estimates, including significantly elevated MCP-1 levels when compared with their normotensive counterparts (152 pg/mL [146–158] and 175 pg/mL [157–193]; P=.009). This may further support the usefulness of using MCP-1 as a biomarker of early vascular deterioration. In the present study population, the significantly higher MCP-1 levels in black men and women than whites is an important finding. The elevated MCP-1 in apparently healthy blacks may indicate that on a vascular endothelial level, the early processes of cellular activation of specific immunological functions are already stimulated[36] and are accompanied by oxidative stress (supported by increased ROS levels). These processes may contribute to early vascular aging and predisposition for the development of hypertension.[2]

A prominent finding from the present study is the positive association between cIMT and MCP-1 in the black women. Possible reasons for this standout finding may be explained by better characterizing this specific group. The black women presented with an increased inflammatory profile (MCP-1, C-reactive protein, and IL-6) and a consistent and independent positive association between cIMT and VCAM-1 (Table III). (We have also confirmed in the present analysis that upon exclusion of black women with masked hypertension, the independent relationships of cIMT with MCP-1 and VCAM-1 remained robust.) Increased levels of MCP-1, hsCRP, IL-6, and VCAM-1 are all established independent risk factors for atherosclerosis and coronary heart disease development.[37] The positive association of cIMT with MCP-1 and VCAM-1 may be an indication of early endothelial cell activation during the initial stages of subclinical atherosclerosis, as MCP-1 promotes the accumulation of lipids in the subendothelial intimal layer.[18] Dansky and colleagues[38] suggested a major role for VCAM-1 in the initiation of atherosclerosis through its recruitment of monocytes to the arterial intima and early foam cell formation. Although the lipid profile of the black women was more favorable compared with the white women, the black women had lower HDL-C values (P<.001). HDL-C promotes cholesterol efflux from the vascular wall and is inversely associated with CVD risk.[39] Added to this, HDL-C inhibits inflammation associated with the development of atherosclerosis.[40] The lower HDL-C of the black women may therefore indicate a decreased cardioprotective effect and increased oxidative stress, which is confirmed by their higher ROS levels (P=.003). Increased ROS in black South Africans has been previously reported[41] and has been linked with endothelial cell activation, dysfunction, and inflammation.[42]

The black women in this study further presented with higher GGT levels (P=.001), although their self-reported alcohol use was similar to the white women. Elevated GGT levels also associate strongly with the development of CVD,[43] and apart from the association of GGT with excessive alcohol intake, it is influenced by factors such as age, obesity, and nonalcoholic fatty liver disease (NAFLD).[44] Furthermore, obesity is most prevalent among South African black women, who are at a greater risk for developing NAFLD.[44] In addition, both overweight and NAFLD status are known to be associated with MCP-1.[45] Although the black women in our study were young, they presented higher obesity indices than whites, and may already be at risk for developing the metabolic syndrome, accompanied by NAFLD, inflammation, and its associated CVD risk.[46]

Where hypertension is traditionally an important risk factor in black South Africans, this population presents with lower incidences of atherosclerosis and coronary heart disease.[47] However, as a result of rapid urbanization and associated dietary and lifestyle changes, the cardiovascular profiles of black South Africans are deteriorating at a greater pace compared with whites.[48] This may lead to an increased burden of atherosclerotic disease in urban blacks. Our finding of early independent associations of cIMT with MCP-1 and VCAM-1 may suggest that these young women form part of a new generation of black South Africans with elevated atherosclerotic disease risk.

The relationships between inflammation, endothelial dysfunction, early vascular deterioration, and arterial stiffness are well established, although the precise sequence of events is complex.[37] Increased arterial stiffness is an independent predictor of CVD and therefore an important endpoint for determining cardiovascular risk.[7,8] In older populations, blacks have been shown to have increased arterial stiffness compared with whites and therefore greater cardiovascular risk.[30,33] Although there was no difference in cfPWV between our young black and white groups, it may be important to note that in addition to their higher central SBP and MCP-1 levels, only cfPWV in the black men and women was positively associated with age. This may suggest early arterial aging in the black group and

TABLE III. Multiple Regression Analyses With MCP-1 as an Independent Variable

	Standard β (95% CI) cfPWV	*P* Value	cIMT	*P* Value
Black men				
R^2/adjusted R^2	0.260/0.161		0.101/–	
bMAP	**0.401 (0.29–0.51)**	**.001**	0.146 (0.02–0.27)	.24
Age	**0.250 (0.13–0.37)**	**.039**	0.100 (−0.03 to 0.23)	.45
MCP-1	0.001 (−0.11 to 0.11)	.99	0.107 (−0.02 to 0.23)	.39
TNF-α	0.004 (−0.11 to 0.11)	.97	−0.020 (−0.14 to 0.11)	.87
VCAM-1	0.011 (−0.09 to 0.12)	.92	0.053 (−0.07 to 0.17)	.66
ROS	0.093 (−0.02 to 0.21)	.39	−0.079 (−0.19 to 0.04)	.51
LDL-C	−0.169 (−0.29 to −0.05)	.17	0.127 (−0.01 to 0.26)	.36
Glucose	−0.108 (−0.22 to 0.01)	.34	−0.111 (−0.24 to 0.01)	.38
Waist circumference	−0.031 (−0.15 to 0.09)	.81	−0.195 (−0.33 to −0.06)	.16
White men				
R^2/adjusted R^2	0.398/0.308		0.127/0.009	
bMAP	**0.511 (0.39–0.63)**	**<.001**	−0.015 (−0.15 to 0.12)	.91
Age	0.129 (0.02–0.24)	.24	0.131 (0.01–0.25)	.29
MCP-1	0.113 (−0.01 to 0.23)	.35	−0.004 (−0.14 to 0.13)	.98
TNF-α	0.076 (−0.03 to 0.18)	.48	0.081 (−0.04 to 0.21)	.51
VCAM-1	−0.048 (−0.16 to 0.06)	.67	−0.215 (−0.34 to −0.09)	.09
ROS	−0.067 (−0.18 to 0.04)	.55	−0.034 (−0.16 to 0.09)	.79
LDL-C	0.029 (−0.08 to 0.13)	.78	−0.028 (−0.15; 0.09)	.82
Glucose	0.117 (−0.82 to 1.1)	.28	0.036 (−1.08 to 1.11)	.77
Waist circumference	0.055 (−0.06 to 0.17)	.65	−0.199 (−0.34 to −0.06)	.15
Black women				
R^2/adjusted R^2	0.273/0.184		0.238/0.151	
bMAP	**0.267 (0.16–0.38)**	**.016**	**0.309 (0.21–0.42)**	**.005**
Age	**0.396 (0.28–0.51)**	**.001**	0.118 (0.01–0.23)	.29
MCP-1	−0.138 (−0.24 to −0.03)	.19	**0.248 (0.14–0.35)**	**.021**
TNF-α	−0.122 (−0.23 to −0.02)	.25	−0.051 (−0.16 to 0.05)	.63
VCAM-1	−0.086 (−0.19 to 0.02)	.43	**0.251 (0.14–0.36)**	**.022**
ROS	−0.0006 (−0.11 to 0.11)	.99	0.069 (−0.04 to 0.17)	.51
LDL-C	−0.072 (−0.18 to 0.04)	.51	0.079 (−0.03 to 0.19)	.46
Glucose	−0.034 (−0.14 to 0.07)	.75	−0.197 (−0.31 to −0.09)	.07
Waist circumference	**−0.241 (−0.35 to −0.13)**	**.036**	−0.152 (−0.26 to −0.04)	.18
White women				
R^2/adjusted R^2	0.134/0.059		0.054/–	
bMAP	**0.328 (0.22–0.44)**	**.003**	0.111 (−0.01 to 0.22)	.33
Age	0.171 (0.08–0.27)	.078	0.126 (0.03–0.23)	.21
MCP-1	−0.009 (−0.11 to 0.09)	.93	−0.012 (−0.11 to 0.09)	.91
TNF-α	−0.099 (−0.19 to −0.01)	.31	0.073 (−0.03 to 0.17)	.46
VCAM-1	−0.028 (−0.12 to 0.07)	.77	0.141 (0.04–0.24)	.16
ROS	−0.077 (−0.17 to 0.02)	.43	0.141 (0.04–0.24)	.17
LDL-C	−0.015 (−0.11 to 0.08)	.88	0.023 (−0.08 to 0.12)	.82
Glucose	0.116 (0.02–0.21)	.22	0.037 (−0.06 to 0.13)	.71
Waist circumference	−0.086 (−0.21 to 0.03)	.46	−0.127 (−0.25 to −0.01)	.29

Abbreviations: bMAP, brachial mean arterial pressure; cfPWV, carotid-femoral pulse wave velocity; CI, confidence interval; cIMT, carotid intima-media wall thickness; LDL-C, low-density lipoprotein cholesterol; MCP-1, monocyte chemoattractant protein-1; ROS, reactive oxygen species; TNF-α, tumor necrosis factor α; VCAM-1, vascular cell adhesion molecule-1.

Bold values indicate $P<.05$.

support previous findings of increased arterial stiffness profiles seen in the South African black population at older ages.[14,33]

STUDY STRENGTHS AND LIMITATIONS

This study must be interpreted within the context of its strengths and potential limitations. MCP-1 is a well-established biomarker or indicator of vascular function and hypertension,[17–19] with an important role in the early development of atherosclerosis.[17,37] Although ethnic differences in cardiovascular inflammatory markers do exist,[14] little is known about MCP-1 levels in different ethnic groups, especially in young and apparently healthy adults. Our findings therefore contribute

to our understanding of the role that chemokines may play in early vascular deterioration in blacks. Our study population consisted of young, apparently healthy men and women, which limits the possibility of a link between large artery structure and function with MCP-1, or to investigate these associations in hypertensive individuals. The cross-sectional study design may be a further limitation as association does not prove cause and effect. The present results form part of a substudy within the larger African-PREDICT study, which may present a further limitation.

CONCLUSIONS

We found that cIMT was independently and positively associated with MCP-1 and VCAM-1 in young apparently healthy black women, but not in black men or in white men and women. Significantly elevated central SBP and MCP-1 concentrations in black compared with white individuals suggest that despite normotensive brachial BP, young Africans may be at increased risk for early vascular deterioration and development of hypertension at younger ages.

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