

# Are Any Changes in Carotid Intima–Media Thickness Associated with Cardiometabolic Risk Among Adult Bantu Central African Hypertensive Patients from Monkole and Biamba Marie Mutombo Hospitals?

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**Background:** Several classic/traditional risk factors are associated with intima–media thickness (IMT), a novel risk of cardio metabolic risk (CMR) in the literature but not in Kinshasa, a megacity prone to CMR. Thus, the objective of this study was to evaluate potential correlations between inflammation, kidney function, psychological stress, hemodynamics, and changes in IMT.

**Methods:** This cross-sectional study was carried out between 2018 and 2021 within Monkole and Biamba Marie Mutombo Hospitals, respectively, and randomly selected from 10 health structures from East and West of Kinshasa, Capital of Democratic Republic Congo (DRC). A random sample of adult hypertensive Bantu Central Africans was examined after bivariate correlations and multiple linear regression.

**Results:** Out of 280 patients with 140 men and 140 women aged  $62 \pm 11$  years, the mean carotid intima–media thickness (CIMT) was  $1.06 \pm 0.5$  mm and 73% ( $n = 204$ ) patients had uncontrolled hypertension. After controlling for confounders, 52.9% variations ( $R^2$ ) of CIMT were independently and significantly ( $P = 0.037$ ) predicted by CRP, 24-hour proteinuria, urinary albumin/creatinine ratio, duration of hypertension, heart rate, hip circumference, and psychological stress with Equation  $Y = 0.717 + 0.87 \times \text{CRP} + 0.02 \times 24 \text{ H} - \text{proteinuria} + 0.005 \times \text{urinary albumin/creatinine ratio} + 0.05 \times \text{duration of hypertension} + 0.001 \times \text{heart rate} + 0.006 \times \text{hip circumference} + 0.017 \times \text{psychological stress}$ .

**Conclusion:** There is an urgent need to control inflammation, impaired renal function, cardiac rhythm, peripheral obesity, longer duration of hypertension management, and stress, which are emerging as specific novel determinants of the subclinical atherosclerosis for those Bantu Central African hypertensive patients.

**Keywords:** carotid intima–media thickness, subclinical atherosclerosis, Central Africans

## Introduction

The Evidence-based Medicine defines cardiometabolic risk (CMR) as a clustering of several traditional cardiovascular risk factors (genetics, aging, obesity, physical inactivity, psychological stress)<sup>1–3</sup> and emerging novel cardiovascular risk factors (environmental, chronic kidney disease, and carotid intima–media thickness/CIMT, inflammatory, hemodynamic, infectious, metabolic and pharmacological/toxic).<sup>4–9</sup>

Sub-Saharan Africa, including the Democratic Republic of Congo (DRC), is also vulnerable to classic/traditional cardiometabolic risk factors (arterial hypertension, obesity, diabetes mellitus, hyperlipidemia, advancing age, smoking, psychological stress and sedentary lifestyle)<sup>1–3</sup> and in the face of emerging risk factors (thrombogenic conditions, homocysteine, markers of inflammation and infection, heredity (discomfort and susceptibility), chronic kidney disease and structural markers (medical imaging for CIMT/subclinical atherosclerosis without plaque versus overt clinical atherosclerosis with plaque).<sup>2,10–12</sup>

However, the reliable, predictive and reproducible measurement of some traditional and new CMR factors to predict differently increasing the CIMT on ultrasound is not yet better defined in hypertension, which is often severe and uncontrolled in Black Bantu Central Africans from Congolese clinical practice.<sup>13</sup>

Thus, the objective of this study was to evaluate potential correlations between inflammation, kidney function, psychological stress, hemodynamics, and changes in IMT.

This is what justified the initiation of the present study with the objective of establishing the variations of the thickening of the CIMT in hypertensive patients at high cardiometabolic risk in a hospital environment in Kinshasa.

## Materials and Methods

This cross-sectional study was carried out between September 2018 and January 2021 within Monkole and Biamba Marie Mutombo Hospitals, respectively, and randomly selected from 10 health structures from East and West of Kinshasa, Capital of DR Congo. A random sample of adult hypertensive Bantu Central Africans was examined after bivariate correlations and multiple linear regression.

A total of 280 consecutive hypertensive patients (50% male,  $\geq 45$  years old) participated in the study. This sample size was sufficient to test all study hypotheses at 5% significance level with 80% power ( $\beta = 0.80$ ).

A convenience sampling procedure was followed to select subjects. The available lifestyle data included self-reported alcohol and smoking habits. Patients who drank alcohol or smoked cigarettes regularly were considered drinkers and smokers. Data were also available for the duration of hypertension, family and personal history of diabetes, hypertension, and current antihypertensive medications.

Atherogenicity indices included CT/HDL-c, TG/HDL-c, LDL-c/HDL-c ratio, Body Fat Index, Visceral Adiposity Index), Height-Obesity Index.<sup>14,15</sup>

After 5 minutes of relaxation, seated blood pressure (BP) was measured at each subject's left arm using an Omron MI digital electronic blood pressure monitor/pulse monitor (OMRON Corporation, Tokyo); 3 BP measurements were taken and averaged for analysis.

According to the SEH/SEC 2018 guidelines, hypertension was defined as BP  $\geq 140/90$  mm Hg or current use of antihypertensives regardless of BP level.<sup>16</sup>

All patients had the following measurements after 12 hours of fasting: total cholesterol (TC), high-density lipoprotein (HDL), triglycerides, blood glucose, serum creatinine, uric acid and CRP.

Cholesterol (Cholesterol Test Kit, Wybenga and Pileggi-One Step Method, Span Diagnostics Ltd) and Triglycerides (Triglyceride Test, GPO-PAP Enzymatic Method, Span Diagnostics Ltd) were measured using enzymatic methods. Low-density lipoprotein-cholesterol (LDL) was calculated according to Friedewald.<sup>17</sup> The Combur test was used to assess proteinuria. Turbidimetry with automatic analyzer was used for CRP.

Metabolic syndrome was defined according to the NCEP-ATP III criteria as, in addition to hypertension, two of the following: waist circumference  $>88$  cm in women and  $>102$  cm in men (central obesity), triglycerides  $\geq 1.69$  mmol/L, HDL  $< 1.30$  mmol/L in women and  $< 1.04$  mmol/L in men, glucose  $\geq 6.11$  mmol/L.<sup>18</sup>

We estimated the glomerular filtration rate (GFR) using four variables, kidney disease diet modification equation (MRAMR)<sup>19</sup> and creatinine clearance (Cl Cr) using Cockcroft's formula-Gault (CG).<sup>20</sup>

Reduced renal function was defined as a GFR  $< 60$  mL/min/1.73 m<sup>2</sup> or a Cl Cr  $< 60$  mL/min according to the guidelines of the Kidney Disease Outcomes Quality Initiative.<sup>21</sup> A B-mode carotid ultrasound was performed for each patient by a qualified physician at the Center Hospitalier Mère et Enfant (CHME) Monkole, Biamba Marie Mutombo Hospital (HBMM) to determine the CIMT.

Carotid intima-media thickness was measured at the level of the distal wall of two common carotid arteries, two centimeters upstream of the bifurcation, over a length of 10 to 20 mm using two high-definition ultrasound scanners (Acuson NX 3 from Siemens and Voluson E8 from General Electric) in Mode B with a high-frequency linear probe of 12 MHz associated with a construction system with multi-incidence scans in order to reduce artefacts and increase the dynamics of contrast.<sup>22,23</sup>

Using automatic wall detection software loaded onto the system, carotid peak and mean IMT values were obtained. An elevation of the CIMT was defined as a CIMT > 0.8 mm and < 1.49 mm according to the generally accepted threshold [35] or >75th percentile (0.8 mm). The patients were finally classified into two groups according to their CIMT: patients with CIMT > 0.8 mm and those with CIMT ≤ 0.8 mm.

## Statistical Analysis

The categorical variable (sex) was presented as frequency (n) and proportion (%).

The others were summarized as mean ± standard deviation with extremes.

The bivariate correlation between the qualitative independent variables and the dependent variable CIMT was calculated using the Pearson coefficient (r) in the case of normal distribution of the quantitative variables.

The multivariate analysis of the multiple linear regression type with a stepwise ascending strategy was used to calculate the variations of the CIMT predicted by certain significant variables in the bivariate correlation after excluding certain confounding variables from the equation.

A value of P < 0.05 was considered significant for the differences.

All analyses were entered and performed using SPSS (the Statistical Package for the Social Sciences) version 26 software for Windows (IBM Inc., Chicago, Illinois, USA).

## Results

A total of 280 patients including 50% of men (n = 140) and 50% of women (n = 140) were examined for essential arterial hypertension, including 73% of cases of uncontrolled hypertension (n = 204).

The mean CIMT was 1.06 ± 0.5 mm with the extreme (0.2 mm minimum and 1.20 mm maximum).

Except for IMG, HDL and height not correlated (P > 0.05) with variations in CIMT, the rest of the quantitative variables were significantly (P < 0.05) correlated with variations in CIMT (Table 1).

After adjusting for confounding factors (SBP, body weight, fasting glucose, CT/HDL-c, TG/HDL-c, TT/T), exclude from the multiple linear regression model equation, only CRP, 24-hour proteinuria, urinary albumin/creatinine ratio, duration of hypertension, radial pulse, hip circumference and number of children were retained as independent, important and significant variables (P < 0.05) predicting 52.9% (R<sup>2</sup>, P change = 0.037) changes in CIMT (Table 2), Figures 1 and 2.

Thus, the regression line calculating the equation Y (CIMT predicted by the following Co variables) = 0.717 + 0.87 + 0.02 + 0.008 + 0.015 + 0.01 + 0.006 + 0.017.

## Discussion

The present study identified emergent factors and conventional/classical factors of carotid atherosclerosis in hypertensive patients across the city of Kinshasa (DRC).

Emerging factors: inflammation (CRP) and renal dysfunction (24-hour proteinuria and albumin/creatinine ratio) were the most powerful covariates according to their bivariate coefficient/multivariate coefficient to predict the increase in CIMT in Bantu patients who are often vulnerable to severe arterial hypertension.<sup>10,24–26</sup>

The present study corroborated the results of the epidemioclinical and carotid echo-Doppler literature, which recently established one of the serum markers of inflammation and an independent and important cardiovascular risk factor.<sup>3,10,27,28</sup>

This cardiometabolic and syndromic risk includes vascular dysfunctions (dysfunctions) (raised blood pressure and endothelial dysfunction), hyperglycemia-insulin resistance (abnormal glucose tolerance, fasting hyperglycemia and type 2 diabetes mellitus), a pro thrombotic and vascular inflammation, abdominal obesity and atherogenic dyslipidemia.<sup>4,6,29–31</sup>

In addition, emerging cardiometabolic risk factors not yet well understood are thrombogenic conditions, homocysteine, markers of inflammation and infection, heredity (discomfort and susceptibility), chronic kidney disease, and

**Table 1** Bivariate Correlations Between the Explanatory Variables and the Variations of the CIMT in the Study Population

Explanatory Variables	Change in CIMT	P
	r-value	
Age (years)	-0.029	0.629
Number of children	0.163	0.006
MV duration (year)	0.432	< 0.0001
SBP (mm Hg)	0.230	< 0.0001
DBP (mmHg)	0.053	0.381
PPP (mmHg)	0.232	< 0.0001
Pulse (beats/min)	0.138	0.021
Weight (Kg)	0.278	< 0.0001
TT (cm)	0.278	< 0.0001
TH (cm)	0.289	< 0.0001
Fasting blood glucose (mg/dl)	0.439	< 0.0001
24h proteinuria (g/24h)	0.444	< 0.0001
Albumin/Creatinine (mg/gr)	0.503	< 0.0001
PCR (mg%)	0.533	< 0.0001
TC (mg/dl)	0.190	< 0.0001
HDL-c (mg/dl)	-0.006	0.919
LDL-c (mg/dl)	0.209	< 0.0001
TG (mg/dl)	0.209	< 0.0001
BMI (%)	0.089	0.137
TG/HDL-c	0.212	< 0.0001
TT/T	0.235	< 0.0001
Cut	0.107	0.073

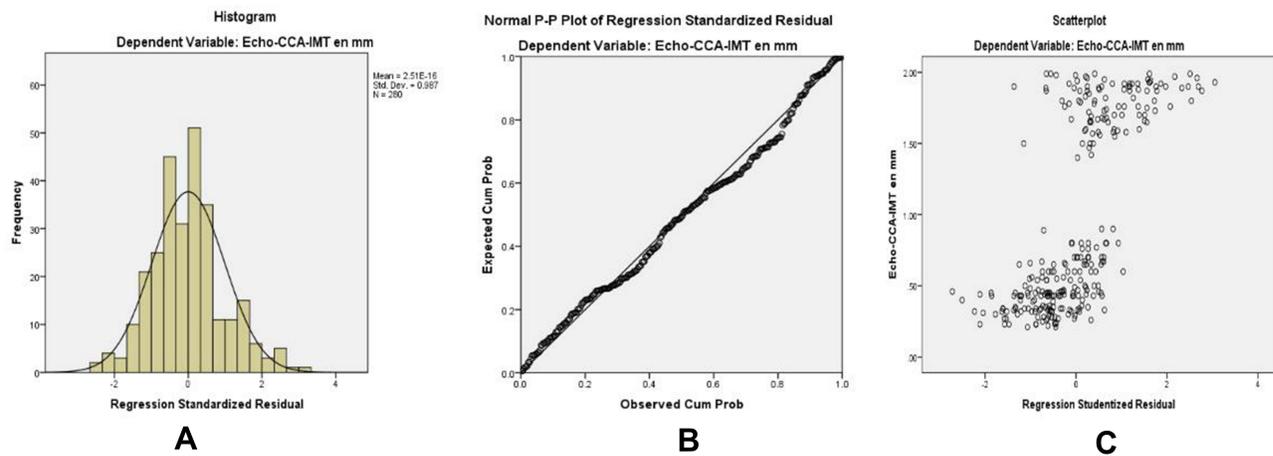
**Table 2** Multiple Linear Regression of Variables Predicting Variations in the CIMT

Variables	B	Standard Error	P	CI
PCR (mg%)	0.87	0.014	< 0.0001	[0.055–0.110]
24h proteinuria (g/24h)	0.002	< 0.0001	< 0.0001	[0.001–0.003]
Albumin/Creatinine (mg/gr)	0.005	0.002	< 0.0001	[0.012–0.503]
Duration of hypertension (year)	0.015	0.004	< 0.0001	[0.008–0.022]
Radial pulse (beat/min)	0.001	< 0.0001	0.008	[0.000–0.002]
TH (cm)	0.006	0.002	0.014	[0.001–0.011]
Number of children	0.017	0.008	0.037	[0.001–0.033]

structural markers (medical imaging: thickening/CIMT/subclinical atherosclerosis without plaque versus manifest clinical atherosclerosis with plaque).<sup>10,32–34</sup>

The global burden of CMR is highlighted by many longitudinal epidemiological studies:<sup>35</sup> 17.5 million people with CMR in 2005 being projected to 23.6 million in 2030.<sup>36,37</sup>

Renal dysfunction, recently recognized and reported in the literature,<sup>38</sup> is characterized by an elevation of 24-hour proteinuria and of the albumin/creatinine ratio was identified as an independent, important and significant predictor of the increase in the CIMT in the present study mainly in Japanese men,<sup>39,40</sup> in the Taiwanese population<sup>41,42</sup> and in elderly non-hypertensives.



**Figure 1** Draws the histogram of the distribution of the CIMT according to the standardized (A) and reproducible regression (B) corresponds to the expected cumulative probability of variations in the CIMT (C).

Indeed, male gender, advancing age, physical inactivity, very low HDL, abdominal obesity, inflammation, Asian ethnicity, smoking, excess alcohol, and albumin ratio/creatinine are, respectively, associated with an increase in the CIMT.<sup>30,43,44</sup>

The increase in values (duration of hypertension, radial pulse, hip circumference and number of children) and classic cardiovascular risk factors for atherosclerosis<sup>45–47</sup> has also demonstrated a very significant multivariate association with proportionally direct increase in the CIMT in the present study.<sup>26,48</sup>

Besides emerging risk factors for atherosclerosis such as elevated CRP/inflammation, proteinuria and elevated albumin/creatinine ratio/kidney dysfunction, the present study also confirmed a significant association between cardiovascular risk factors. Classical cardiometabolic/atherosclerosis risk such as systolic blood pressure, pulse pressure, weight, waist circumference, hip circumference, hyperglycemia, total cholesterol, LDL-cholesterol, triglyceride, circumference of the height (TT)/height (T), TG/HDL-cholesterol and the increase in EIMc.<sup>10,32,49</sup>

In the middle of sub-Saharan Africa, poverty and political instability<sup>38,48,50</sup> worsen uncontrolled hypertension.<sup>38,51</sup>

The constellation of cardiometabolic risk and the coexistence of advancing age as a pro-oxidant factor<sup>52</sup> with classic and/or emerging atherogenic risk factors in uncontrolled urbanization coupled with health transitions (epidemiological, demographic and nutritional) promote subclinical atherosclerosis measured by the elevation of the CIMT in the present study.<sup>53–58</sup>

## Implications of Carotid Bioimaging

Current results will have implications for routine practice, education, capacity building and research in the pre-diagnosis of atherosclerotic and metabolic diseases in Kinshasa.

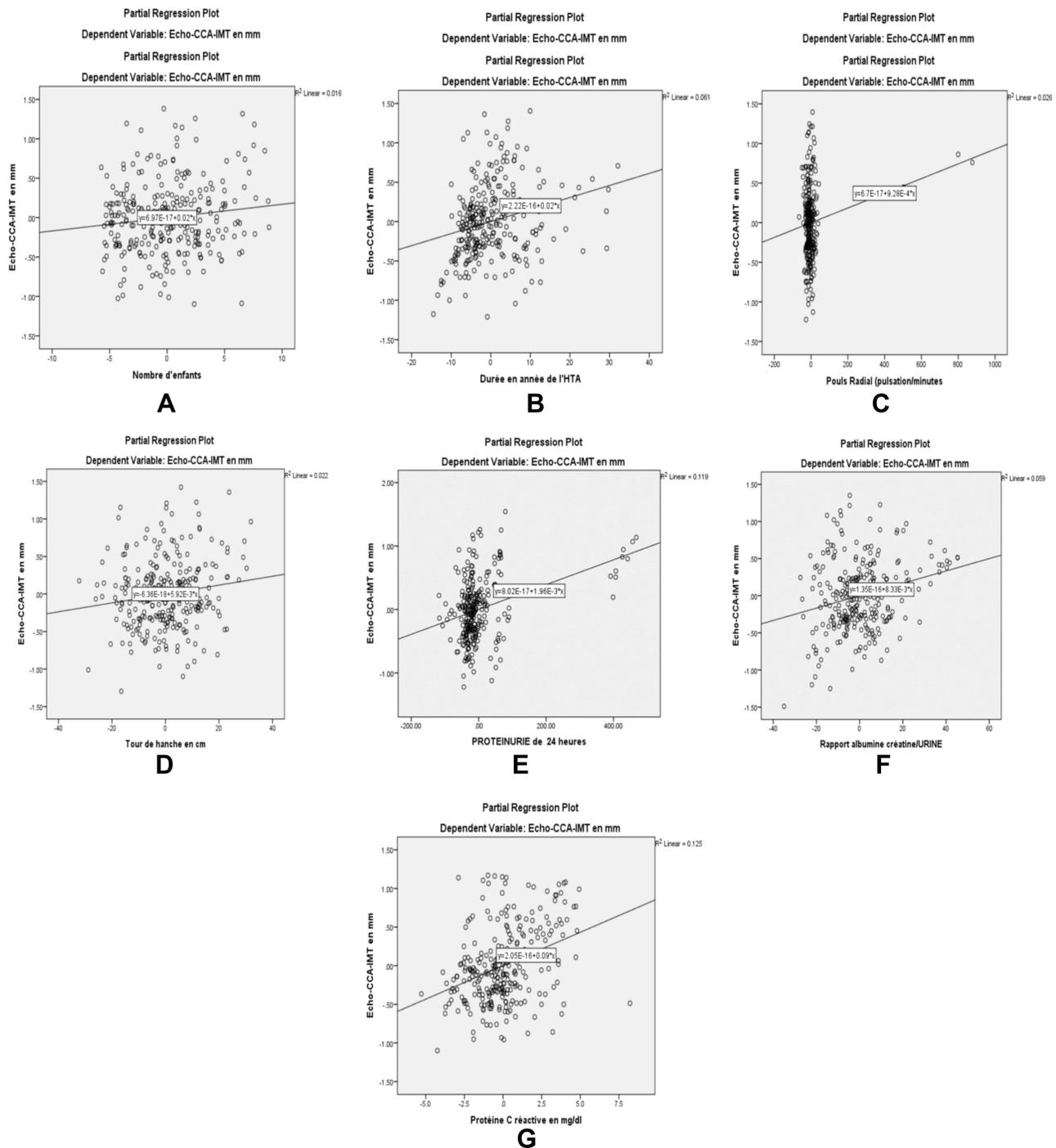
There is an urgent need to convince Congolese political, academic and scientific decision-makers to anticipate personalized early medicine, precision medicine, participatory medicine (involvement of the community and patients), evidence medicine, preventive medicine and political governance.<sup>10,59</sup>

Indeed, the radiologist and the clinician are invited to adopt a holistic and integrative approach to the thickening of the carotid intima media at all levels of the health system (primordial, primary, secondary, tertiary and quaternary).

## Strength and Limitations of the Study

The strength of this study lies in the courage to carry out the first work around subclinical atherosclerosis and biomarkers of inflammation, hemodynamics, obesity, dyslipidemia and renal dysfunction in the Democratic Republic of the Congo (DRC).

However, the limits of this work reside in the absence of follow-up of patients at high cardiometabolic risk in hypertensives, essential predictors of overt clinical atherosclerosis.<sup>26,60,61</sup>



**Figure 2** Corresponds to the expected cumulative probability of variations in the CIMT. Figures draw the different regression lines showing the number of children (**A**), the duration in years of hypertension (**B**), the radial pulse (**C**), the Hip circumference (**D**), the 24-hour proteinuria (**E**), the urinary albumin/creatinine ratio (**F**), and the significant multivariate correlations between the CIMT and the CRP (**G**).

## Ethical Considerations

To carry out this study, the protocol was submitted to the scientific committee of the Department of Internal Medicine of the University Clinics of Kinshasa and to the ethics committee of the School of Public Health of the University of Kinshasa acting as the national ethics committee (Approval number: ESP/CE/076/2018).

After explanation of the objectives of the study, its progress, its safety and its merits, an informed consent was obtained from the participants in the study while respecting confidentiality in accordance with the Helsinki protocol.

## Conclusion

There is an urgent need to control inflammation, Impaired renal function, cardiac rhythm, peripheral obesity, longer duration of hypertension management, and stress, which are emerging as specific novel determinants of the subclinical atherosclerosis for those Bantu Central African hypertensive patients.

## Disclosure

The authors report no conflicts of interest in relation to this work.

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