Association of HIV, cardiovascular risk factors, and carotid intimal media thickness
A cross-sectional study in Western Kenya

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The carotid intimal media thickness (CIMT) is a validated measure of subclinical atherosclerosis. Human immunodeficiency virus (HIV) is a risk factor for cardiovascular disease (CVD) and has been associated with CIMT in North America and Europe; however, there are limited data from Sub-Saharan Africa (SSA). In this cross-sectional study, we measured CIMT in a cohort of 262 people living with HIV (PLHIV) on antiretroviral therapy (ART) for ≥6 months and HIV-negative adults in western Kenya. Using linear regression, we examined the associations between CVD risk factors and CIMT, both overall and stratified according to the HIV status. Among the PLHIV, we examined the association between CIMT and HIV-related factors. Of 262 participants, approximately half were women. The HIV-negative group had a higher prevalence of age ≥55 years (P = .002), previously diagnosed hypertension (P = .02), treatment for hypertension (P = .03), and elevated blood pressure (BP) (P = .01). Overall prevalence of carotid plaques was low (15/262 [6.0%]). HIV-positive status was not significantly associated with a greater mean CIMT (P = .19). In multivariable regression models, PLHIV with elevated blood pressure or treatment for hypertension had a greater mean CIMT (P = .002). However, the CD4 count, viral load, and ART regimen were not associated with differences in CIMT. In the HIV-negative group, older age (P = .006), high total cholesterol levels (P = .01), and diabetes (P = .02) were associated with a greater mean CIMT. In this cross-sectional study of Kenyan adults, traditional CVD risk factors were found to be more prevalent among HIV-negative participants. After multivariable regression analysis, we found no association between HIV status and CIMT, and PLHIV had fewer CVD risk factors associated with CIMT than HIV-negative participants did. HIV-specific factors were not associated with the CIMT.

Abbreviations: ART = Antiretroviral therapy, BP = blood pressure, BMI = body mass index, CIMT = carotid intimal media thickness, CVD = cardiovascular disease, HDL = high density lipoproteins, HIV = human immunodeficiency virus, HTN = hypertension, LDL = low density lipoproteins, MI = myocardial infarction, PLHIV = people living with HIV, SSA = Sub-Saharan Africa.

Keywords: Cardiovascular risk factors, carotid intimal media thickness, disease, human immunodeficiency virus, Western Kenya

1. Introduction
Human immunodeficiency virus (HIV) infection is associated with a nearly two-fold increased risk of cardiovascular disease (CVD).[1,2] Contributing factors include increased chronic inflammation and immune activation associated with HIV infection,[3,4] traditional CVD risk factors, and antiretroviral therapy (ART), particularly regimens including protease inhibitors (PIs).[5,6,7] Worldwide, there are now a greater number of people living with HIV (PLHIV), with the majority living in
Sub-Saharan Africa (SSA).[6,7] Given the large and increasing global burden of CVD,[12] clinical tools are needed to improve risk stratification and management of CVD for PLHIV in SSA, which is reliable, feasible, and cost-effective.

In longitudinal studies in North America and Europe, carotid intimal media thickness (CIMT) has been validated as an indicator of subclinical atherosclerosis and a predictor of future CVD events, such as stroke and myocardial infarction (MI).[13,14] Carotid plaque, a focal lesion in the arterial wall that can impede blood flow, is also recognized as a marker of subclinical atherosclerosis and a predictor of CVD independent of CIMT.[10] CIMT varies by age, race, and sex; however, carotid plaques may be present even when CIMT does not increase.[11-13] Both CIMT and the presence of carotid artery plaque can be assessed noninvasively using ultrasound. This provides an advantage for screening for the presence of subclinical CVD over more invasive and costly procedures, such as coronary angiography.

In a large meta-analysis and systematic review of observational studies that included PLHIV, a higher CIMT was associated with HIV-positive status.[16,19] However, most of these studies were from regions with low HIV prevalence, such as Europe or North America, and greater use of protease inhibitors (PIs) than other antiretroviral drugs.[16,18] In a small number of cross-sectional studies from SSA, an association between PLHIV and greater CIMT has not been uniformly observed. Thus, given the higher prevalence of HIV in SSA as well as the different environmental and genetic factors that confer risk for CVD, more work is needed to determine the relationships between abnormal CIMT, HIV, and CVD risk factors in SSA to efficiently target interventions for individuals at the highest risk.

In this study, we evaluated the association between HIV status and CIMT in a rural setting in western Kenya with a high HIV prevalence. We also examined the association between CIMT risk factors and CIMT when stratified by HIV status. Finally, we examined the association between CIMT and HIV-specific factors such as HIV viral load and CD4 count.

2. Methods

2.1. Study design and setting

The parent study enrolled PLHIV and HIV-negative men and women living in western Kenya and was conducted in collaboration with the University of Washington, University of Nairobi, Kenya National Hospital, and Kenya Ministry of Health. Participants were enrolled at the Kisumu Sub-County Hospital in Kisumu County, which serves the surrounding communities in Western Kenya. The main study matched participants according to HIV status and sex, enrolling 150 PLHIV men, 150 PLHIV women, 149 HIV-negative men, and 149 HIV-negative women. The eligibility criteria were at least 30 years old and living within a 50 km radius of the hospital. PLHIV had to be enrolled and regularly attended the HIV comprehensive care clinic and used ART for a minimum of six months. PLHIV who met the inclusion criteria and consented to participate in the study were enrolled by a comprehensive care clinic study nurse. HIV-negative participants were recruited from hospital HIV testing sites until the required sample size was achieved.

Human subject approval was obtained from the University of Washington Institutional Review Board and the Kenya National Hospital/University of Nairobi Ethical and Scientific Review Committee. All the participants provided written informed consent.

2.2. Study procedures

The detailed procedures for this cross-sectional study have been published.[16] We collected subject health and demographic data using the World Health Organization STEP wise approach to Surveillance (STEPS) questionnaire[17] modified for the Kenyan context. This included a self-reported history of cardiovascular risk factors and physical examination. Blood pressure (BP) was recorded twice in each arm, five minutes apart, using a digital sphygmomanometer (CH 453, Omron Health). Anthropometric measurements included height, weight, and waist circumference. Participants returned after an initial visit for carotid ultrasound and fasting blood tests for lipid, glucose, and HIV-specific factors such as viral load and CD4 count.

2.3. CIMT ultrasound examination

Radiographers at Kisumu County Referral Hospital received training in scanning techniques, acquisition, and interpretation of images using a Sonosite M Turbo ultrasound machine (FUJIFILM, Sonosite Inc., Bothell) with an HFL38X/13-6 MHZ transducer. Training and quality assurance for radiographers was provided by FM, a radiologist experienced in performing carotid ultrasound and measurement of CIMT for research purposes.[18] The standard operating procedures for this study were based on protocols for the measurement of CIMT from the American Society of Echocardiography.[19] The Sonosite software program (SonoCalc v5.0.0.12) was used for image acquisition and reporting. Intrarreader reliability was assessed during training, but not made available.

Examination of the extracranial carotid arteries included identification of carotid plaques and measurement of CIMT in both the right and left common carotid arteries. First, the study participant was positioned in a semi-upright position with the head slightly tilted to the left or right depending on the side being examined. The common carotid artery (CCA) was identified with the ultrasound probe in the longitudinal position using a proximal point 10 mm from the carotid bulb. Measurements of intima-media thickness were taken with the ultrasound probe in the anterior, posterior, and lateral positions, and three measurements of the mean IMT segment, calculated automatically by the software, were made at the near and far vessel walls (6 in total). The combined average of all measurements was reported as the overall CIMT for the common carotid artery in a similar study.[11] A mean CCA IMT >1.5 mm at any of the measured points was considered a plaque.

Ultrasound images of each participant were recorded, stored, and transferred after each examination. The research radiologist assigned to training (FM) performed the subsequent reading and reporting of the studies, and a formal report was generated using SonoCalc v5.0.0.12. In total, only 262 participants had a formal report verified for inclusion in the final analysis due to funding limitations. These participants were selected via consecutive sampling and matched by age, sex, and HIV status. The smaller sample size was calculated to be adequately powered to detect significant differences in the CIMT.

2.4. Definition of dependent and independent variables

Independent variables included the following demographic and lifestyle factors: age, sex (male or female), smoking status (current = smoking within 12 months and ex-smoker ≥12 months without use), and educational level (no formal schooling, primary schooling, secondary school completed, or more than secondary school). CVD history included a self-reported prior diagnosis of hypertension (HTN), HTN treatment, diabetes treatment, and prior MI or stroke. We classified hypertension according to the Kenyan hypertension guidelines adopted from the Eighth Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC VIII).[20] We used the Consensus Criteria 2009 for metabolic syndrome (MetS)[21] to define the following: elevated total cholesterol (TC) > 200 mg/dL, elevated low-density lipoprotein (LDL-C) > 130 mg/dL, reduced high-density lipoprotein (HDL-C) (for women < 50 mg/dL and
for men < 40 mg/dL, elevated triglycerides (TG) > 150 mg/dL, and abdominal obesity (waist circumference > 88 cm for women and > 94 cm for men). We defined diabetes as a fasting blood glucose level ≥ 126 mg/dL or use of oral hypoglycemic agents, as per the World Health Organization recommendations.[12] HIV status as an independent variable, as well as duration of ART (years), current CD4 count (cells/mm³), nadir CD4 count (cells/mm³), suppressed viral load (<50 copies/mL), and ART regimen (either protease-first-line vs non-protease inhibitor-second-line regimen). CIMT was analyzed as a continuous dependent variable.

2.5. Sample size and statistical analysis

This study was powered to detect a minimum mean CIMT difference of 0.04 mm with 80% confidence enrolling a minimum of 110 PLHIV and 110 HIV-negative patients. This reference mean difference in CIMT was also used in another SSA study[23] and reported in a large systematic review of observational studies[14] and in a later study that compared PLHIV in the fat redistribution and metabolic changes in HIV infection (FRAM) study with HIV-negative patients in the Multi-Ethnic Study of Atherosclerosis (MESA).[15,24]

Categorical baseline characteristics were compared between PLHIV and HIV-negative individuals using the chi-squared or Fisher’s exact tests. Given the small sample size in each subgroup, we classified age, education, and body mass index (BMI) as binary variables: age (<55 vs ≥55 years), education level (below or above the secondary level), and BMI (<25 or ≥25 kg/m²). The blood pressure was calculated as the average of all readings. CIMT was analyzed as a continuous variable and was normally distributed. Linear regression was used to assess the association between independent variables and CIMT for the entire cohort, which was then stratified by HIV status. Residual plots were used to assess the validity of these four assumptions. There were 21 outliers in the CIMT dataset. These outliers were validated with the corresponding CIMT reports and were not excluded as they were not influential. Missing data were excluded from analysis.

Initially, simple linear regression models were used to assess the association between an independent variable and CIMT, first with the entire cohort, and then stratified by HIV status. In the multivariable regression model, the independent variables (P ≤ .15) in the simple linear regression models were included, as well as variables of clinical significance that a priori included age, sex, and education status. The multivariable model was conducted with backward regression and stepwise removal of variables, until the best model fit was obtained. Statistical significance was set at P < .05. All statistical analyses were conducted using the R software (version 3.6.1 [RStudio Team (2020). RStudio: Integrated Development for R. RStudio, PBC, Boston, MA]).

3. Results

3.1. Demographic and clinical characteristics

Of the 262 participants, 145 were PLHIV negative and 117 were HIV negative (Table 1). The proportion of those ≥55 years was lower in the PLHIV than in the negative group, 40% versus 59%, respectively (P = .02). Women comprised over half of the PLHIV positive and HIV negative participants (P = .02). Older age, ≥55 years) was associated with a of 0.05 mm higher CIMT (95% CI: 0.01, 0.07), compared to those with a normal range LDL-C (95%CI: −0.001, 0.08, P = .06), although this was borderline in terms of statistical significance. Finally, a diagnosis of diabetes was associated

4. Traditional CVD risk factors and CIMT in the cohort

4.1. Simple linear regression analyses

Overall, several factors were significantly associated with CIMT in simple linear regression models using data from the entire cohort, including HIV status, older age, elevated blood pressure and/or use of antihypertensive agents, and diabetes (Table 2).

HIV positive status was associated with a 0.03 mm lower CIMT (95% confidence interval [CI]: −0.01, 0.07) compared to those who were HIV negative (P = .02). Older age, ≥55 years) was associated with a of 0.05 mm higher CIMT (95% CI: 0.01, 0.07), compared to those ≥55 years of age (P = .004). Those with elevated LDL-C had a 0.04 mm higher mean CIMT, compared to those with a normal range LDL-C (95% CI: −0.001, 0.08, P = .06), although this was borderline in terms of statistical significance.
with a 0.12 mm higher mean CIMT in comparison to those without a diagnosis of diabetes (95% CI: 0.02, 0.22, P = .02).

4.2. Multivariable regression analysis

The independent variables in the model included older age, female sex, secondary education, ex-smoking status, high blood pressure or hypertension treatment, elevated TC and LDL-C levels, and diabetes (Table 2). After adjustment, HIV-positive status was not significantly associated with greater CIMT (P = .19). Significant associations were seen in those who were older with a 0.03 mm higher CIMT (95% CI: 0.001, 0.07, P = .04) and in those with a diagnosis of diabetes with a 0.11 mm higher CIMT, compared to those without diabetes (95% CI: 0.008, 0.21, P = .02).

5. Traditional CVD risk factors and CIMT stratified by HIV status

5.1. Simple linear regression analysis

Among PLHIV (Table 3), those with elevated blood pressure or on HTN treatment had a 0.06 mm higher mean CIMT compared to those with a normal range blood pressure or not on treatment (95% CI: 0.02, 0.11, P = .003). None of the HIV-related factors were significantly associated with CIMT in the simple linear regression analysis.

Several CVD risk factors were associated with a higher CIMT in the HIV-negative group (Table 3). Older age was associated with a 0.07 mm higher mean CIMT (95% CI: 0.02, 0.12, P = .006), those with elevated TC had a 0.08 mm higher mean CIMT (95% CI: 0.02, 0.14, P = .01), and those with an elevated LDL-C had a 0.07 mm higher mean CIMT (95% CI: 0.003, 0.13, P = .04). Finally, those with diabetes had a 0.17 mm higher mean CIMT (95% CI: 0.03, 0.31, P = .02).

5.2. Multivariable linear regression analysis

Among PLHIV (Table 3), the model included older age, female sex, secondary school education, high BP, and use of hypertension treatment. After adjustment, the final model only included those with elevated blood pressure or hypertension treatment that was associated with a 0.07 mm higher mean CIMT (95% CI: 0.02, 0.11, P = .002). Female sex was not significantly associated with CIMT in the final model (P = .08).
In the HIV-negative group (Table 3), the model included older age, female sex, secondary school education, elevated TC and LDL-C levels, and diabetes mellitus. After adjustment, the final model included only older age, elevated TC level, and diabetes. Those Participants who were older had a 0.07 mm higher mean CIMT (95%CI: 0.02, 0.12, P = .006), those with elevated TC had a 0.09 mm higher CIMT (95%CI: 0.03, 0.14, P = .01), and those with diabetes had a 0.17 mm higher mean CIMT (95%CI: 0.03, 0.31, P = .02).

6. Discussion

In this cross-sectional study of Kenyan adults, with a virally suppressed group of PLHIV and a community-matched group of HIV-negative individuals, HIV-positive status was not associated with a higher CIMT after adjusting for other significant CVD risk factors. This lack of association has also been observed in several other studies conducted in SSA where CIMT was measured and is contrary to findings from studies in high-and-middle-income countries that found an association between HIV infection and greater CIMT. Overall, our CIMT values were lower in this cohort than in similar SSA studies. Importantly, we found that some CVD risk factors were associated with higher CIMT among HIV-negative participants, and our results are consistent with other SSA studies that have shown that PLHIV with sustained viral suppression do not show a difference in CIMT, as well as from other low-middle-income countries (LMICs) suggesting that well-controlled HIV infection may not be a significant risk factor for early CVD in SSA. This also supports the need for longitudinal studies to better understand the relationships among HIV, CVD risk factors, and CVD morbidity, specifically in SSA, to support targeted interventions.

Our study findings in PLHIV compare to a study by Muiru et al (2018) that reported a significantly lower mean CIMT in PLHIV than in HIV-negative patients (0.62 mm vs 68 mm). PLHIV also had lower CVD risk scores, smoking prevalence, and median systolic blood pressure in this cohort. The four center H3 Africa-HW1 Gen Study reported an overall age and sex mean adjusted CIMT of 64 mm with a statistically different mean CIMT between centers: the highest CIMT at the Ghana site and lowest in Agincourt, one of the South African (SA) sites (0.69 mm vs 60 mm). The prevalence of HIV in the H3 study varied from <1% to 35%. HIV status was self-reported in some centers but was associated with lower CIMT along with high HDL-C and current alcohol consumption. After adjustment for age, education status, education status, and traditional CVD risk factors in the pooled analysis. We observed a lower overall mean CIMT than these studies and low overall plaque prevalence that did not differ by HIV status. Our results are similar to the Ndlovu cohort, which reported a carotid plaque prevalence of 4.5% that did not differ by HIV status, but different from a Botswana study, which reported a higher plaque prevalence in PLHIV (15% in PLHIV vs 7% in HIV-negative persons). This may reflect better management of cardiovascular risk factors in SSA countries, or other lifestyle or environmental factors that were not measured in this study.

In addition, the measurement of CIMT and definition of subclinical atherosclerosis vary across studies. Some have defined subclinical atherosclerosis as a CIMT ≥0.78 mm, a criterion derived from a European longitudinal study tracking initial media thickness of children with familial hypercholesterolemia and healthy comparators. We did not use this definition because it has not been validated in SSA and very few participants had a CIMT above this threshold. Additional
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PLHIV has also been observed in other studies [38] including a levels were more prevalent in PLHIV. Hypertriglyceridemia in

and the use of different measures, such as maximum CIMT

ting ultrasound scan techniques, sex distribution, study size,

†Final regression model for HIV-negative: older age;

Definitions: elevated BP ≥ 140 mm Hg or ≥ 90 mm Hg. Elevated BMI (≥25 kg/m²), abdominal obesity = waist circumference >88 cm for women and >94 cm for men. Elevated TC >200 mg/dL. Elevated

CoLVH (n = 145)*

HIV-neg (n = 117)†

β coefficient (95%CI) P value

β coefficient (95%CI) P value

Demographic variables

Age ≥55 yr 0.01 (−0.02, 0.03) .50

Female sex 0.03 (−0.006, 0.07) .10

Lifestyle factors

Current smoker −0.02 (−0.12, 0.08) .65

Ex-smoker 0.04 (−0.02, 0.09) .23

Secondary education −0.02 (−0.06, 0.02) .26

CVD history

Hypertension 0.03 (−0.03, 0.09) .36

Physical exam

Elevated BP or on treatment 0.06 (0.02, 0.11) .003* 0.02 (−0.04, 0.09) .49

Anthropometric factors

Elevated BMI 0.004 (−0.04, 0.04) .84

Abdominal obesity (males) −0.020 (−0.09, 0.09) .96

Abdominal obesity (males) −0.002 (−0.09, 0.09) .96

Laboratory measurements

Elevated TC −0.01 (−0.05, 0.04) .72

Elevated LDL-C 0.01 (−0.05, 0.06) .81

Reduced HDL-C (males) −0.004 (−0.05, 0.04) .87

Reduced HDL-C (males) 0.002 (−0.08, 0.08) .95

Elevated TG −0.02 (−0.08, 0.04) .52

Diabetes 0.01 (−0.15, 0.17) .90

HIV related factors

Duration on ART (yr) 0.0004 (−0.004, 0.004) .86

CD4 count (current) 0.005 (−0.04, 0.05) .79

CD4 count (nadir) −0.003 (−0.04, 0.03) .86

Undetectable VL −0.02 (−0.06, 0.02) .38

ART 2nd line regimen (PI) 0.003 (−0.05, 0.05) .88

We also observed several cardiovascular risk factors in the cohort that were positively associated with CIMT in the multivariable regression model. In the HIV-negative group, older age, high TC levels, and diabetes were associated with a higher CIMT. These findings have also been observed in other SSA studies and in studies of low-to-middle-income countries.[23,34,35] Interestingly, elevated blood pressure was not positively associated with CIMT in this group despite the significantly higher prevalence of reported HTN (P = .02). However, self-reported use of hypertension treatment was also higher (P = .03) than in PLHIV.

Of note, our finding of a positive association between elevated blood pressure and hypertension treatment with CIMT in the PLHIV group in the multivariable regression model was interesting given the younger median age, lower prevalence of self-reported hypertension, hypertension treatment, and lower prevalence of elevated blood pressure compared to the HIV-negative group. Smoking prevalence was low overall, and we did not find a significant difference in the prevalence of higher BMI, central obesity, or dyslipidemia between the groups, except for the higher prevalence of hyperglycemia in PLHIV. A possible explanation may be that PLHIV may have increased markers of endothelial dysfunction despite longstanding viral suppression.[28,40–43] This may contribute to a higher CIMT in the context of under-reporting of hypertension treatment and BP status. Measurement of inflammatory markers such as IL-6 and C-reactive protein might further support this hypothesis.

We did not observe an association between ART and CIMT. The lack of association has also been observed in some other factors that may make study comparisons difficult include differing ultrasound scan techniques, sex distribution, study size, and the use of different measures, such as maximum CIMT rather than the overall mean in some cohorts.[31,37]

In our study, we observed a greater prevalence of CVD risk factors in the HIV-negative group, notably older age, a history of hypertension, hypertension treatment, and elevated blood pressure. This was also true in the main study[16] which included younger individuals, where the prevalence of MetS did not find a significant difference in the prevalence of higher reported HTN (P < .01). However, self-reported use of hypertension treatment was also higher (P = .03) than in PLHIV.

We did not observe an association between ART and CIMT. The lack of association has also been observed in some other

Table 3

Factors associated with differences in CIMT stratified by HIV status with simple and multivariable regression.*†

| Demographic variables | PLHIV (n = 145)* | HIV-neg (n = 117)† |
|-----------------------|-----------------|-----------------|
| β coefficient (95%CI) | P value         | β coefficient (95%CI) | P value         |
| Age ≥55 yr            | 0.01 (−0.02, 0.03) | .50             | 0.07 (0.02, 0.12) | .006**         |
| Female sex            | 0.03 (−0.006, 0.07) | .10             | 0.01 (−0.04, 0.06) | .66            |
| Current smoker        | −0.02 (−0.12, 0.08) | .65             | −0.01 (−0.11, 0.09) | .78            |
| Ex-smoker             | 0.04 (−0.02, 0.09) | .23             | 0.03 (−0.04, 0.11) | .36            |
| Secondary education   | −0.02 (−0.06, 0.02) | .26             | −0.01 (−0.06, 0.04) | .57            |
| Hypertension          | 0.03 (−0.03, 0.09) | .36             | 0.02 (−0.04, 0.09) | .49            |
| Elevated BP or on treatment | 0.06 (0.02, 0.11) | .003*           | 0.01 (−0.04, 0.07) | .59            |
| Elevated BMI          | 0.004 (−0.04, 0.04) | .84             | −0.03 (−0.09, 0.02) | .16            |
| Abdominal obesity (males) | −0.01 (−0.04, 0.06) | .81             | 0.01 (−0.07, 0.08) | .87            |
| Abdominal obesity (males) | −0.002 (−0.09, 0.09) | .96             | −0.06 (−0.17, 0.04) | .23            |
| Elevated TC           | −0.01 (−0.05, 0.04) | .72             | 0.08 (0.02, 0.14) | .01**          |
| Elevated LDL-C        | 0.01 (−0.05, 0.06) | .81             | 0.07 (0.005, 0.13) | .04            |
| Reduced HDL-C (males)  | −0.004 (−0.05, 0.04) | .87             | −0.04 (−0.12, 0.04) | .28            |
| Reduced HDL-C (males)  | 0.002 (−0.08, 0.08) | .95             | −0.06 (−0.14, 0.02) | .16            |
| Elevated TG           | −0.02 (−0.08, 0.04) | .52             | 0.08 (−0.05, 0.20) | .21            |
| Diabetes              | 0.01 (−0.15, 0.17) | .90             | 0.17 (0.03, 0.31) | .02**          |

Definitions: elevated BP ≥ 140 mm Hg or ≥ 90 mm Hg; Elevated BMI (≥25 kg/m²), abdominal obesity = waist circumference >88 cm for women and >94 cm for men; Elevated TC >200 mg/dL; Elevated LDL-C >130 mg/dL and Elevated TG >150 mg/dL; Reduced HDL-C <50 mg/dL in women and <40 mg/dL in men. Diabetes (WHO) was defined as fasting glucose ≥126 mg/dL or hypoglycemic agents. HIV related factors; Suppressed VL < 1000 copies/mL; Undetectable VL <50 copies/mL.

95% CI = 95% confidence interval; ART = antiretroviral therapy, BMI = body mass index, BP = blood pressure, CD4 = cluster differentiation 4, CVD = cardiovascular disease, DBP = diastolic blood pressure, HDL = high-density lipoprotein, HIV = human immunodeficiency virus, HTN = hypertension, LDL = low-density lipoprotein, MI = myocardial infarction, PI = protease inhibitor, SBP = systolic blood pressure, TGs = triglyceride.

Final regression model for PLHIV: female sex; β coefficient =−0.03 ([95%CI: −0.004, 0.004], P = .08); elevated BP or on HTN treatment (β coefficient =0.07 ([95%CI:0.02,0.11], P = .002**). *Indicates significance in the final model and not shown in table.

Final regression model for HIV-negative: older age; β coefficient =0.07 ([95% CI:0.01,0.12], P = .01**); elevated BP or on HTN treatment (β coefficient =−0.04 ([95%CI:−0.09,0.15], P = .14); high TC; β coefficient =0.09 ([95%CI:0.03,0.14], P = .01**); diabetes; β coefficient =0.21 ([95% CI: 0.08,0.34], P = .002**). **Indicates those that were significant in the final model and not shown in table.
SSA and LMIC studies,[12,13,35] but a more recent SSA study found an association when stratified by age between the time spent on PLHIV on ART[27] and the HIV-negative study group (in those >30 years of age).

Finally, the findings of the association of fewer CVD risk factors with higher CIMT in PLHIV in this study suggest that PLHIV may have better access to and engagement in medical care and education on lifestyle modification within the HIV comprehensive care system (1), highlighting the importance of primary prevention of CVD risk factors in the general population. It should be noted that the use of statins and aspirin, the mainstays of primary prevention of CVD in high-income countries, was almost nonexistent across the cohort.

The strengths of this study include the use of a HIV-negative comparator group as a baseline to assess the relationship between CVD risk factors and CIMT in a community-based cohort. We also used validated measures of the carotid artery to obtain CIMT measurements.

Limitations include the cross-sectional study design, which does not permit analysis of the progression of subclinical atherosclerosis and the effect of treatment of CVD risk factors and HIV disease management. Following the study, we were unable to review the scans independently to ascertain intra and inter-reader reliability due to technical issues which was also a limitation. Self-reporting of cardiovascular risk factors, such as a history of hypertension and diabetes, as well as the use of medications to treat these conditions, was a further limitation of this analysis. Although this study was appropriately powered to detect significant differences in CIMT, it was smaller than the original cohort, and despite matching by age, sex and HIV status, the HIV-negative group is older. However, we adjusted for this in the analysis and did not see a significant difference in CIMT.

In our study, we did not observe a significant association between HIV status and CIMT, after adjusting for other known CVD risk factors. We observed a higher prevalence of some CVD risk factors in the HIV-negative group, and associations between some of these CVD risk factors and CIMT. These findings are supported by other SSA studies that observed more significant associations between CVD risk factors and higher CIMT in HIV-negative groups and may reflect better access to medical care and support for PLHIV in SSA. Our CIMT measurements and plaque prevalence were lower than those in other studies and may be due to differing study population factors, sampling techniques, study design and/or CIMT quantification techniques. However, inclusion of more participants in our cohort with a longer follow up period might demonstrate results that are similar to other SSA studies with respect to CIMT.

Although there are some limitations to the study design, these results add to the body of literature, highlighting the importance of the primary prevention of CVD in the general population. Identifying the most consistent and powerful tool to quantify the CVD risk for PLHIV in SSA will require larger studies and may be due to differing study population factors, techniques. However, inclusion of more participants in our cohort with a longer follow up period might demonstrate results that are similar to other SSA studies with respect to CIMT.

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Supplementary material

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