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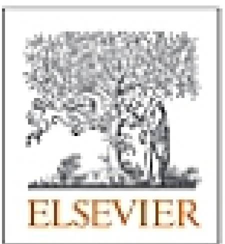

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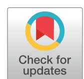
ORIGINAL ARTICLE

Frequency and factors associated with arterial remodeling in persons living with human immunodeficiency virus in Parakou in 2019



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KEYWORDS
Arterial remodeling;
Atherosclerosis;
Human immunodeficiency virus;
Epidemiology;
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Summary
Background. — The side effects of antiretroviral drugs and the chronic inflammation induced by human immunodeficiency virus (HIV) infection contribute to the development of atherosclerotic arterial remodeling in people living with HIV (PLWH).
Objectives. — To determine the frequency and factors associated with arterial remodeling in PLWH treated at the university hospital of Parakou.
Methods. — It was a cross-sectional, descriptive, and analytic study. Data were collected from March to August 2019 at the university hospital of Parakou in Benin. PLWH aged at least 18 years and consenting were included. The diagnosis of arterial remodeling was retained in the presence of at least one of the following criteria: carotid intima-media thickness $\geq$ 1 mm, anteroposterior diameter of the abdominal aorta $\geq$ 25 mm, ankle brachial index < 0.9, presence of atheromatous plaque. Data were recorded and analyzed with R 3.5.1 software, and the threshold of significance was 5%.

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Results. — A total of 114 patients have undergone arterial Doppler ultrasound. The majority were women (71.9%). The patients' mean age was 43.2 ± 10.2 years with extremes of 18 and 67 years. The frequency of arterial remodeling was 24.6%. The most common atherosclerotic lesion found was atheromatous overload (IMT ≥ 1 mm). Age ≥ 50 y (p = 0.003; ORa = 4.9[1.5—15.6]), male sex (p = 0.037; ORa = 4.1[1.3—13.4]), and a family history of hypertension and/or diabetes (p = 0.027; ORa = 3.6[1.1—12.8]) were significantly associated with atherosclerosis in PLWH.
Conclusion. — Arterial remodeling was frequent among PLWH in Parakou in 2019. The associated factors were the classic cardiovascular risk factors that should be systematically taken into account in the follow-up of these patients.
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Introduction

Cardiovascular diseases (CVDs) are the leading cause of death worldwide with an estimated number of deaths of 17.7 million meaning 31% of total global mortality in 2016 [1]. These CVDs include coronary artery disease, stroke, peripheral vascular disease and heart failure. Many factors contribute to these diseases. In addition to the traditional cardiovascular risk factors that are already known, infectious diseases especially viral diseases (hepatitis B and C (HVB and HVC) and human immunodeficiency virus (HIV) infection), have been associated with CVDs [2—5]. In fact, in people living with HIV (PLWH), the use of antiretroviral therapy (ART) has contributed to a significant reduction in mortality from opportunistic infections, resulting in an increase in the life expectancy of these patients. This increase in life expectancy of PLWH associated with the side effects of ART has led to the emergence of cardiovascular complications. These include arterial remodeling, most commonly from atherosclerotic origin [6—8]. Several studies have addressed the issue of atherosclerosis among PLWH. In South Africa, the prevalence of subclinical atherosclerosis among PLWH was 12% in 2015 [9]. Increasing prevalence has been found in the literature. For example, this prevalence was 18% in Uganda in 2014 [10], 33.6% in Croatia in 2013 [11], 64.7% in Côte d'Ivoire in 2018 [12] and 67.6% in Ghana in 2019 [13].

In Parakou (Benin), the incidence of peripheral artery disease (PAD) among PLWH was 31.16% in 2016 [14]. This high incidence of PAD in this study is probably the expression of higher atherosclerotic disease in this group of persons. Thus, to help improve the care of PLWH, we report on the frequency and distribution of arterial remodeling and associated factors in these patients in Parakou in 2019.

Patients and methods

Framework, type and period of study

The study took place in the internal medicine department of the Departmental-Borgou/Alibori University Hospital Center (CHUD-B/A), in the municipality of Parakou. This hospital, located 415 km from Cotonou (economic capital of Benin), is one of the greatest HIV treatment sites in northern Benin.

The study was cross-sectional, descriptive and analytical. Data were collected from March 31, 2019 to August 31, 2019.

Study population

The study covered all PLWH who consulted during the study period. We systematically included all PLWH at least aged 18 and who gave their consent. Were excluded from the study, those for whom arterial Doppler ultrasound could not be performed.

Variables of interest

The dependant variable was arterial remodeling. It was sought in the supra-aortic trunks, abdominal aorta and arteries of the lower limbs. The diagnosis of arterial remodeling was made at the Doppler ultrasound according to the following criteria:

- at the supra-aortic trunks: intima media thickness (IMT) ≥ 1 mm and/or presence of atherosclerotic plaque defined as IMT > 1.5 mm [8,15—17];
- in the abdominal aorta: the presence of atheroma plaques and/or an abdominal aorta diameter > 25 mm (ectasia if diameter between 25—30 mm and aneurysm if diameter 30 mm with loss of wall parallelism) [18];
- at the level of the arteries of the lower limbs: the Ankle Brachial Index (ABI) < 0.9 and/or the presence of plaque at the level of the arterial network of the lower limb [19].

For each atherosclerotic plaque found at any site, the different characteristics were described. These characteristics were: diffusion (unilateral; bilateral), location, number, echogenicity (anechogenic; hypoechogenic, isoechogenic, hyperechogenic), structure (homogeneous; heterogeneous), plaque surface (regular, irregular) and degree of stenosis in percentage [20].

The independent variables were socio-demographic characteristics (age, sex, and occupation), cardiovascular risk factors (high blood pressure, smoking, diabetes, dyslipidemia, and obesity), family history of hypertension, diabetes and the characteristics of HIV infection and those of ART :

- hypertension was retained in patients with systolic blood pressure (SBP) ≥ 140 mmHg and/or diastolic blood pressure (DBP) ≥ 90 mmHg on at least two of the three consecutive measurements separated by an interval of one minute each and/or patient under antihypertensive treatment and/or patient known as hypertensive [21];

- all patients who are currently using tobacco (regardless of the method of use) or who have stopped smoking for less than three years have been considered as smokers [21];
- general obesity was defined as a body mass index (BMI) $\geq$ 30 kg/m^2 [22]. Abdominal obesity was appreciated by waist circumference greater than or equal to 94 cm in men or greater than or equal to 80 cm in women [22];
- sedentary lifestyles were held in patients who did not participate in daily physical activity or who participated in physical activity lasting less than 120 minutes per week [21];
- patients who were known as diabetics or who were under antidiabetic treatment or whose fasting glucose was greater than 1.26 g/L were considered as diabetic. Hyperglycemia was restricted to fasting blood glucose between 1.10 and 1.26 g/L in subjects with no history of diabetes [17];
- dyslipidemia was defined by: total cholesterol (TC) > 2 g/L and/or triglycerides (TG) > 1.5 g/L and/or HDL cholesterol (HDL-C) < 0.40 g/L and/or LDL cholesterol (LDL-C) > 1.30 g/L. LDL-C was determined using Friedwald's formula: LDL cholesterol (g/L) = total cholesterol (g/L) - HDL cholesterol (g/L) -1/5 of triglycerides (g/L). The following abnormalities were distinguished: total hypercholesterolemia (TC > 2.00 g/L), HDL hypocholesterolemia (HDL-C < 0.40 g/L), LDL hypercholesterolemia (LDL-C > 1.30 g/L), hypertriglyceridemia (TG > 1.50 g/L) with normal cholesterolemia, mixed hyperlipidemia: CT > 2.00 g/L and TG > 1.50 g/L [17,21—23];
- metabolic syndrome was defined according to the International Diabetes Federation [24] criteria by abdominal obesity associated with two (2) or more of the following four (4) other criteria:
  - hypertriglyceridemia: TG > 1.5 g/L,
  - HDL-C hypocholesterolemia (< 0.40 g/L in men and < 0.50 g/L in women),
  - hypertension: SBP $\geq$ 130 mmHg or DBP $\geq$ 85 mmHg or treatment of previous diagnosed hypertension,
  - hyperglycemia $\geq$ 1.10 g/L or known diabetes;
- the overall cardiovascular risk level (CVD) was estimated based on the Framingham score [25];
- family history of stroke or early myocardial infarction was considered if stroke occurred before the age of 45 in a family member or if myocardial infarction occurred before the age of 50 in a male parent or 60 in a female parent.

Data collection

After obtaining the necessary authorizations, the purpose of the survey was explained to the patients. They were recruited individually after giving their written informed consent to participate in the survey. Socio-demographic characteristics and certain cardiovascular risk factors were collected during a face-to-face interview using a structured questionnaire. A physical examination of each patient was conducted with anthropometric measurements. The data collected during the physical examination and the various measurements taken had been used to fill out part of the survey sheet. Using the PLWH follow-up medical record, we supplemented the survey sheet with information on HIV, its management and the value of the last blood sugar level. After this step, an appointment was given to each patient for blood collection, lipid assessment and completion of the arterial Doppler ultrasound. The results of the lipid assessment were then recorded in the fact sheet for each patient.

Ankle Brachial Index Measurement

Ankle Brachial Index (ABI) was obtained by the ratio of systolic to ankle blood pressure (ABP) to brachial systolic blood pressure bilaterally [19]. These pressures were measured using an electronic OMRON blood pressure monitor with small, medium and large cuffs. On each side, systolic arterial pressures were measured in a patient lying down for at least 15 minutes, away from the meal or taking an exciting (coffee, cigarette, alcohol). Three successive measurements were taken one minute apart [21]. The average of the last two measures was used to calculate the ABI. The side where the ABI value was the lowest was selected for the study.

Vascular ultrasound measurement

Arterial ultrasound-Doppler assessments (carotid, abdominal aorta and lower limb) were performed by a cardiologist for all patients using a Sonoscape SSI-8000 Doppler echocardiograph with a cardiac and vascular probe. In case of abnormality, the exam is confirmed by another cardiologist.

The intima media thickness (IMT) was measured in accordance with the Mannheim consensus protocol [15]. Thus, three successive manual measurements of IMT were made at the common carotid artery 10 mm upstream of the bifurcation, both on the left and on the right. An average was averaged on each side. The side where the IMT average was highest was used as the patient's value. The aorta was examined in the longitudinal plane and then in the axial plane. We measured the maximum anteroposterior diameter at the supra-renal and infra-renal levels. Three consecutive measurements were made at each stage and the calculated mean of the measurements was taken as the diameter of the aorta [18].

The results of the arterial ultrasound-Doppler assessment were recorded directly in the investigation sheets for each subject. The fact sheets were completed by a medical doctoral student for all patients.

Statistical analysis

Data collected were entered with epidata version 3.1.fr software, cleared and then analyzed with R version 3.5.1 software. Qualitative variables were described in proportion and quantitative variables in mean with the standard deviation or in median with the interquartile interval depending on whether the distribution was normal or not. The proportions were compared with the Pearson Chi^2 test or the exact Fisher test as appropriate. The quantitative variables were compared with the Student test or the Kruskal—Wallis test according to whether the distribution is normal or not. A p-value threshold of less than 5% was used for statistically significant associations in univariate analysis. A binary

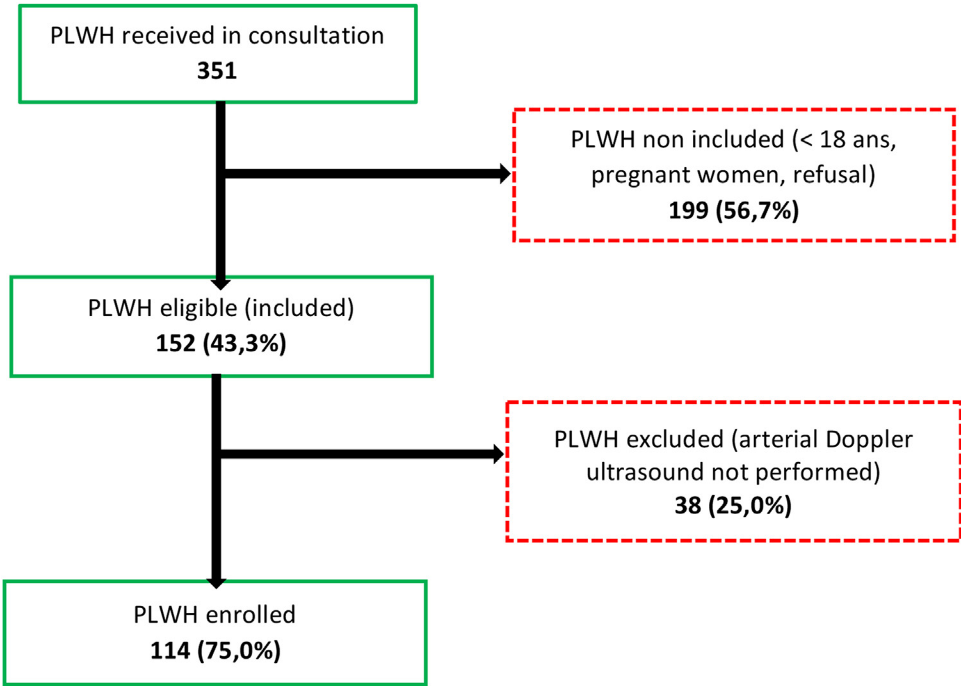

Figure 1 Flow chart showing the selection of people living with the human immunodeficiency virus followed at the Departmental-Borgou/Alibori University Hospital Center (CHUD-B/A) in Parakou in 2019 for the arterial remodeling study. PLWH: People Living With HIV

logistic regression was performed for the adjustment of associated factors in univariate. The initial multivariate analysis model included variables associated in univariate analysis at the p-value < 20% threshold and forced variables theoretically recognized in the literature whose p-value was above the inclusion threshold (forced variables). The variables included in the initial model were age, sex, tobacco use, diabetes, dyslipidemia, overall cardiovascular risk level, high blood pressure, obesity, metabolic syndrome, and a family history of high blood pressure and/or diabetes. The step-by-step regression method was applied and factors associated with a p-value < 5% threshold in the final model were considered to be independently associated with arterial remodeling.

Ethical considerations

This study, which is consistent with the principles set out in the 1975 Declaration of Helsinki [26], was approved by the Local Ethics Council of the University of Parakou under number 224/CLERB-UP/P/SP/R/SA. Informed consent was obtained from all participants.

Results

During the collection period, out of the 351 PLWH consulted, 152 were eligible and included in the study. Of the 152 eligible, 38 were excluded for not receiving an arterial Doppler ultrasound. As a result of the data collection, 114 PLWH were taken into account in our analysis (Fig. 1).

The participation rate was 75%. The mean age in the sample was 43.2 ± 10.2 years with values ranging between 18 and 67 years. Women were predominant (71.9%) with a sex ratio of 0.4. Metabolic syndrome was present in 13.2% of participants. The overall cardiovascular risk estimated by the Framingham score was low in 64%, moderate or medium in 32.5% and high in 3.5% of the subjects surveyed. Table 1 presents the frequency of cardiovascular risk factors observed in patients.

Concerning the HIV infection characteristics, all patients were infected with HIV 1. The co-infections HIV 1&2 and HIV &HBV (hepatitis B virus) were respectively found in two (1.8%) and seven (6.1%) patients. All patients were on antiretroviral therapy (ART). The age of infection and duration of exposure to antiretroviral therapy are shown in Table 2. The other characteristics of HIV infection are presented in Table 3.

Frequency of arterial remodeling and description of lesions

Among the 114 patients included in our analysis, 28 (24.6%) had arterial remodeling. In these patients, the location of the lesions was at the carotid level in all patients (100%) and the lower limbs in 10 patients (35.71%). The abdominal aorta attack was observed in no patients.

In the carotid arteries, the left side's IMT ranged from 0.67 to 1.20 with a median of 1.07; interquartile intervals (1.01;1.20). On the right side, it's from 0.33 to 1.45 with a median of 0.69; interquartile intervals (0.58;0.81). Atheromatous overload was present in 16 patients (57.14%). Atheromatous plaque was found in seven patients (25%). In these seven patients, 12 plaques were found and all had a degree of stenosis of less than 50%.

Table 1 Cardiovascular risk factors observed in people living with the human immunodeficiency virus at the Departmental Borgou/Alibori (CHUD-B/A) University Hospital Center in Parakou in 2019 ($n = 114$).

	Patients (n)	Percentage (%)
Age (years)		
< 50	89	78.1
≥ 50	25	21.9
Sex		
Male	32	28.1
Female	82	71.9
Smoking		
Yes	5	4.4
No	109	95.6
Hypertension		
Yes	29	25.4
No	85	74.6
Diabetes		
Yes	5	4.4
No	109	95.6
Dyslipidemia		
Yes	59	51.8
No	55	48.2
Body mass index (BMI) (kg/m^2)		
< 30	104	91.2
≥ 30	10	8.8
Abdominal obesity		
Yes	74	64.9
No	40	35.1
Sedentarity		
Yes	38	33.3
No	76	66.7
Metabolic syndrome		
Yes	15	13.2
No	99	86.8
Family history of early stroke or myocardial infarction		
Yes	10	8.8
No	104	91.2
Family history of high blood pressure and/or diabetes		
Yes	52	45.6
No	62	54.4
Level of cardiovascular risk according to Framingham score		
Low	73	64.0
Moderate	37	32.5
High	4	3.5

Table 2 Age of infection and duration of exposure to antiretroviral therapy in people living with the human immunodeficiency virus at the Departmental Borgou/Alibori (CHUD-B/A) University Hospital Center in Parakou in 2019 ($n = 114$).

	Minimum (month)	Maximum (month)	Median (Q1; Q3) (month)
Age of infection	1	261	62.5 (33; 114)
Duration of ART treatment	1	206	54.5 (26; 79.5)
Duration of exposure to protease inhibitor	1	96	25.5 (20.5; 37.5)

In the right lower limbs, the ABI ranged from 0.48 to 1.37 with a median of 1.02; interquartile intervals (0.98;1.14). On the left side, the ABI ranged from 0.50 to 1.37 with a median of 1.03; interquartile intervals (0.99;1.14). Peripheral artery disease (ABI < 0.9) was present in 10 patients (8.8%). Of these patients, two had four atheromatous plaques on the ultrasound scan. In all cases the plaques were bilateral, had a homogeneous structure, a regular surface and a degree of stenosis lower than 50%.

Table 3 Characteristics of antiretroviral treatment in people living with the human immunodeficiency virus at the Departmental Borgou/Alibori (CHUD-B/A) University Hospital Center in Parakou in 2019.

	Patients (*n*)	Percentage (%)
Serotype ($n = 114$)		
HIV 1	114	100.0
HIV 2	2	1.8
Current CD4 rate (number/mm^3; $n = 114$)		
> 500	65	56.6
[200—500]	30	26.8
< 200	19	17.0
Viral load ($n = 91$)		
Detectable	19	4.4
Indetectable	72	95.6
WHO stage at initiation of treatment ($n = 114$)		
Early (stage 1 & 2)	41	36
Late (stage 3 & 4)	73	64
Exposure to protease inhibitor ($n = 114$)		
Yes	12	10.5
No	102	89.5
Therapeutic line ($n = 114$)		
Line 1	104	91.2
Line 2	10	8.8

Table 4 Characteristics of the plates of atherom observed in people living with the human immunodeficiency virus at the Departmental-Borgou/Alibori University Hospital Center in Parakou in 2019 ($n = 16$).

	Patients (*n*)	Percentage (%)
Diffusion		
Unilateral	6	37.5
Bilateral	10	62.5
Location		
Common carotid artery	5	31.2
Internal carotid artery	2	43.8
Femoral	2	12.5
Popliteal	2	12.5
Echogenicity		
Hypoechogenic	2	12.5
Hyperechogenic	5	31.2
Isoechogenic	9	56.3
Structure		
Homogenous	15	93.7
Heterogenous	1	6.3
Surface		
Regular	15	93.7
Irregular	1	6.3

Table 4 presents the characteristics of the atheromatous plaques observed in all these patients.

Factors associated with arterial remodeling

In univariate analysis, age, sex, tobacco use, moderate hyperglycemia, high overall cardiovascular risk, and diabetes were significantly associated with arterial remodeling (Table 5).

Factors independently associated with arterial remodeling were age 50 (ORa: 4.9; 95% CI: [1.5—15.6]; $p = 0.003$), male (ORa: 4.1; 95% CI: [1.3—13.4]; $P = 0.037$) and the existence of a family history of high blood pressure and/or diabetes (ORa: 3.6; 95% CI: [1.1—12.8]; $P = 0.027$) (Table 5).

Discussion

Our study aimed to assess the importance of subclinical arterial remodeling in a tropical PLWH population. We

Table 5 Factors associated with arterial remodeling in people living with the human immunodeficiency virus at the Departmental-Borgou/Alibori University Hospital Center (CHUD-B/A) in Parakou in 2019.

	n	Univariate analysis			Multivariate analysis		
		ORb	95% CI	*P*	ORa	95% CI	*P*
Age class (years)				0.001			0.003
< 50	42	1	—		1	—	
≥ 50	72	5.3	[1.3—21.7]		4.9	[1.5—15.6]	
Sex				0.003			0.037
Male	32	4.2	[1.5—11.6]		4.1	[1.3—13.4]	
Female	82	1	—		1	—	
Family history of hypertension and/or diabetes				0.055			0.027
Yes	52	2.6	[0.9—7.1]		3.6	[1.1—12.8]	
No	62	1	—		1	—	

therefore carried out an ultrasound screening through the evaluation of the intima media thickness at the level of the common carotid, the diameter of the abdominal aorta and the systolic pressure index, all recognized markers of atherosclerosis at different vascular sites [27]. For IMT, the thresholds for defining subclinical atherosclerosis are variable. Some studies use a value greater than or equal to 0.78 mm to define carotid atherosclerosis based on the fact that a healthy adult attains an IMT of 0.78 mm at age 76 [28]. We preferred to use the one-millimeter threshold to define atherosclerosis because this threshold is well correlated with cardiovascular events including myocardial infarction [16,17,29]. Although the risk of underestimating the importance of atherosclerosis in this population is high, the frequency we obtained actually reflects the true load of carotid arterial remodeling in PLWH in our series. Based on arterial Doppler ultrasound performed in 114 PLWH with an average age of 43.2 ± 10.2 years and followed in a hospital setting in Parakou, the frequency of arterial remodeling was 17.5%. This remodeling was most often atheroma whose predominant location was carotid. The factors independently associated with arterial remodeling in PLWH were age 50, male and having a family history of high blood pressure and/or diabetes.

Frequency of arterial remodeling

With an IMT threshold of 1 millimeter, we obtained a frequency of 17.5% among our PLWH, all of them under antiretroviral treatment. Using this same threshold, Sarfo et al. in Ghana in 2019 reported a frequency of 21.2%; which frequency increased to 67.6% when applying a 0.78 mm threshold [13]. Also, Aboubakar Djalloh et al. in 2018 in Ivory Coast reported a prevalence of subclinical arterial remodeling of 64.7% in a 201 population of PLWH on ART, including 64.2% of atherosclerosis of supra-aortic trunks [12]. The incidence of atherosclerosis therefore appears to be high in our respective populations (West African) compared to data from other African countries. Indeed, using the 0.78 mm threshold to define carotid atherosclerosis, Ssinabulya et al. [10] in Uganda in 2014 and Schoffelen et al. [9] in 2015 in South Africa, had respectively reported arterial remodeling frequencies of 18% and 12% respectively among PLWH on ART.

Before concluding on the high frequency of arterial remodeling among PLWH in our West African series, we must take into account the small size of our population. Schoffelen's study, for example, included 904 PLWH, whereas we only included 114 patients in our study.

Atherosclerotic lesions appear to be more common among PLWH. Slightly higher IMT values among PLWH compared to healthy subjects were reported by some authors [13,30]. However, most comparative studies in poor countries do not show a higher frequency of arterial remodeling among PLWH [9,10,13,31,32]. Atherosclerosis, on the other hand, is more common among PLWH in rich countries [33—36]. In our study, we did not compare with a negative HIV population and no HIV-related characteristics were found to be associated with arterial remodeling among PLWH. Longitudinal studies, on a larger sample, are needed to verify this association in our population. We already believe that this frequency will be high among PLWH, considering the high frequencies of arterial remodeling that have been reported in specific at-risk populations in Benin [37—39]. In addition, the prevalence of peripheral arterial disease in lower limbs among PLWH in Parakou in 2016 was 31.16% [14], and 34.90% in Cotonou in 2014 [40]. This hypothesis is based on the chronic inflammation observed during HIV infection and the accumulation of conventional cardiovascular risk factors [40].

Factors associated with arterial remodeling in PLWH

In our study, age was associated with arterial remodeling in PLWH. Also, PLWH older than 50 years were more likely to have atherosclerotic lesions. Viškovic et al. in Croatia [11], Schoffelen et al. [9] in South Africa in 2015, Stein et al. [41] in the United States in 2013, Kwiatkowska et al. [42] in Poland in 2011, [43] Albuquerque et al. [43] in Brazil in 2013 and de Mosepele et al. [44] in Botswana in 2017 also reported the association between age and frequency of arterial remodeling among PLWH. These data confirm that advanced age is a potential factor in arterial remodeling regardless of HIV infection. Routine screening for arterial remodeling should be done by the age of 50 for PLWH.

Sex

In our PLWH series, men were more likely to have atherosclerosis than women. This result reflects the fact that, regardless of HIV, male subjects are more vulnerable. In women, estrogens cause an increase in HDL-cholesterol and a decrease in LDL-cholesterol. They also have a direct action on the vascular endothelium and smooth vascular muscle, which results in a decrease in the expression of molecules involved in monocytes adhesion to endothelial cells and a decrease in chemokines responsible for monocytes migration into sub-endothelial space. Thus, the risk of atherosclerosis is lower in women [45]. Albuquerque et al. [43] in Brazil, Parra et al. [30] in Spain also found that men were more likely to develop atherosclerosis.

Tobacco consumption

We observed in our study that tobacco use was associated with arterial remodeling among PLWH. Tobacco consumption is a major cause of arterial remodeling [17,21]. This result goes along with those of Pacheco et al. [32] in Brazil and Grundfield et al. [33] in the United States. In contrast, Jean et al. [46] in France and Kwiatkowska et al. [42] in Poland did not find a significant link between atherosclerosis and tobacco use among PLWH. This could be explained by the fact that in their study population more than half were smokers, 54% and 81.9% respectively, while in our study only 4.4% were smokers.

Diabetes

In line with literature data [33,47], diabetes is associated with arterial remodeling in PLWH. In fact, metabolic disorders (hyperglycemia, lipid disorders, hyperinsulinism) observed in diabetics lead to an acceleration of the onset of arterial remodeling in diabetic patients regardless of HIV infection [48]. Thus, the association of these metabolic disorders with chronic inflammation induced by HIV infection would constitute a double risk of atherosclerosis. In contrast, Sankatsing et al. [49] in Netherlands in 2009 did not find an association between atherosclerosis and diabetes among PLWH. This discrepancy could be explained by a virtual absence of diabetic patients in their study.

Overall high cardiovascular risk (CVR) according to Framingham

Our study showed an overall high CVR according to Framigham that was associated with arterial remodelling in PLWH population. Sankatsing et al. [49] found a relationship between atherosclerosis and the increase in overall CVR according to Framingham. Falcone et al. [50] in the United States as well as Jerico et al. [51] in Spain also found that overall CVR $\geq$ 10% according to Framingham was associated with arterial remodeling among PLWH. The significant association found between atherosclerosis and global CVR according to Framingham through these studies may be due to the fact that the evaluation of global RCV according to the Framingham model takes into account age, sex, total cholesterol and HDL cholesterol levels, blood pressure, smoking and personal history of diabetes. All these factors are known in the genesis of arterial remodeling. Thus, we can say that the assessment of overall CVR is an important tool in predicting the occurrence of arterial remodeling in PLWH.

Characteristics of the HIV infection

In our study, no statistically significant association was found between the time of discovery of HIV infection and atherosclerosis in PLWH. This same observation was also made by Schoffelen et al. [9] and Jean et al. [46]. However, Mosepele et al. [44] in Botswana in 2017 found that the delay in discovering HIV infection was significantly associated with arterial remodeling. This difference could be explained by the fact that the median time to discover HIV infection in our study was relatively shorter (62.5 months versus 120 months in the Botswana study). This relationship with the age of exposure can be understood when one takes into account the observations of Volpe et al. [35], which showed a faster progression of arterial remodeling in PLWH.

Our study also showed that no statistical association was found between viral load and atherosclerosis in PLWH. In contrast, Albuquerque et al. [43] in Brazil found an association between viral load 10,000 copies and atherosclerosis among PLWH. This difference is probably of a methodological nature. In fact, in the multivariate analysis, Albuquerque et al. [43] did not take into account certain confounding factors such as metabolic syndrome, obesity, high blood pressure, smoking and dyslipidemia, which are independent and major risk factors for arterial remodeling.

The duration of ART was not significantly associated with arterial remodeling in PLWH. This result is in line with those of Jean et al. [46] in France in 2016. In contrast, Aboubakar Djalloh et al. [12] in Ivory Coast in 2018, found a relationship between arterial remodeling and the duration of ARV treatment. It should be noted that in this study, the authors included subjects who had been on ARVs for at least six months, whereas in our study only new cases were included. The low representativeness of subjects under ART containing protease inhibitor (PI) in our series could also explain this discrepancy. We did not observe a relationship between PI exposure and atherosclerosis in our patients. This observation was also made by Schoffelen et al. [9] and Jean et al. [46]. In contrary, Sankatsing et al. [49] in the Netherlands, found that atherosclerosis in PLWH was associated with the ART regimen containing PI. Also, according to Maggi et al. [8], PLWH with a therapeutic regimen containing PI had a significantly higher subclinical atherosclerotic load (52.4%) than those on treatment with non-nucleoside reverse transcriptase inhibitors (NNRTI) (15%). Similarly, they reported that the rate of IMT abnormalities was not significantly different between NNRTI-based treatment in HIV patients and HIV-negative Italian controls. In fact, IP are responsible not only for arterial remodeling but also for arterial and venous complications [6,7].

According to the present study, no variables related to HIV infection and its treatment were associated with arterial remodeling, contrary to some literature data. The only associated factors were the traditional risk factors for atherosclerosis.

Study limitation

This study, which is the first in our country evaluating arterial remodeling among PLWH, has certain limitations that must be taken into account. The small size of our population may have reduced the power of our analyses and did not reveal the association between HIV infection characteristics and atherosclerosis. Although the Mannheim consensus protocol was followed during IMT measurements and this measurement was repeated three times in each patient, the involvement of two cardiologists could introduce an inter-observer bias in our measurements. Similarly, the use of an electronic blood pressure monitor for ankle pressure measurement has certainly underestimated the frequency of peripheral arterial disease in the lower limbs and therefore the arterial remodeling that we reported. This under-estimation by conventional automatic blood pressure monitors has been widely demonstrated [52,53]. The MESI ABPI MD Enhanced Electronic Blood Pressure Monitors that enable automated oscillomometer measurement of blood pressure at the ankle appear to be as accurate as Doppler [53,54]. Unfortunately, these devices are not yet available in our community.

Conclusion

The frequency of arterial remodeling was 17.5% among PLWH followed in the internal medicine department at CHUD-B/A in 2019. The factors that were associated with this arterial remodeling were the classic risk factors such as: age 50, male, moderate hyperglycemia, diabetes, tobacco use, Framingham's high overall cardiovascular risk, and family history of high blood pressure and/or diabetes. Thus, the control and consideration of these associated factors can contribute significantly to the reduction of the prevalence of arterial remodeling and the improvement of the health of PLWH in Parakou.

Human and animal rights

The authors declare that the work described has not involved experimentation on humans or animals.

Informed consent and patient details

The authors declare that they obtained a written informed consent from the patients included in the article. The authors also confirm that the personal details of the patients have been removed.

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The authors declare that they have no competing interest.

Author contributions

All authors attest that they meet the current International Committee of Medical Journal Editors (ICMJE) criteria for Authorship.

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Codjo H.L., Houenassi M.: conceptualization, methodology, resources, validation.

Codjo H.L., Dohou S.H.M., Rouga K.D., Amegan H.N., Biaou C.O.A.: formal analysis, investigation, methodology, software, writing, original draft.

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