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Epidemiology of Lower Extremity Artery Disease in People Living with HIV Followed at the Departmental University Hospital Center Ouémé-Plateau in 2019

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Abstract

Introduction: Lower extremity artery disease (LEAD) is a serious cardiovascular disease. People living with the human immunodeficiency virus (HIV) are at risk. The aim of the study was to determine the prevalence of LEAD and identify the associated factors among people living with HIV who were followed at the departmental university hospital Ouémé-Plateau in Benin. **Methods:** This was a cross-sectional study. It included all HIV-infected people who were monitored at the department of medicine of the target hospital during the study period and met the inclusion criteria (followed for at least three months, aged at least 25 years, and having given their written consent to participate). Data were collected during an individual interview, followed by the measurement of parameters. The ankle brachial index ≤ 0.9 was used for the diagnosis of LEAD. Associated factors were searched through a multivariable logistic regression. **Results:** The prevalence of LEAD was 34.2% among 222 respondents having a mean age was 42.9 ± 10.8 years and a female predominance (77.5%). No significant association was found between the presence of LEAD and sociodemographic factors. The presence of LEAD was significantly associated with hypertension and antiretroviral therapy. Hypertensive patients had a higher risk of LEAD compared to non-hypertensive patients (OR = 1.98, 95% CI [1.04 - 3.83], p = 0.037). Those who were receiving second-line therapy also had a higher risk of LEAD compared to those on first-line therapy (OR = 2.95, 95% CI [1.14 - 7.60], p = 0.025). **Conclusion:**

This study showed a high prevalence of LEAD especially among hypertensive patients and those who were receiving second-line antiretroviral therapy. LEAD diagnosis and management should be included in the routine care of people living with HIV in Benin.

Keywords

Lower Extremity Arterial Disease, People Living with HIV, Benin

1. Introduction

Lower extremity artery disease (LEAD) has a high risk of death, disability, and impairment of quality of life. It's a chronic condition with a prolonged, asymptomatic phase. The main cause is atherosclerosis. LEAD shares the same risk factors as coronary diseases, which it can be associated with. Screening is done by measuring the ankle-brachial index (ABI), a non-invasive test [1]. The prevalence of LEAD varies from 2% between 40 - 44 years old to 12% between 70 - 74 years old [2]. Its incidence is increasing in low- or middle-income countries. In Benin, a prevalence of 5.5% was found among adults aged 18 years and over during a study conducted in the Tanvè village in 2017 [3].

Cardiovascular diseases are one of the main causes of morbidity and mortality in people living with the human immunodeficiency virus (PLWH) [4] [5]. Their risk of a cardiovascular event is higher than that of the general population [6]. Human immunodeficiency virus (HIV) infection has a demonstrated atherogenic potential, due to the inflammatory effects of the virus and lipodystrophy secondary to some antiretroviral therapies. In addition, treated PLWH have improved survival with exposure to classic cardiovascular risk factors (smoking, obesity, hypertension, and diabetes) comparable to uninfected people.

HIV infection remains a public health problem in Africa, despite considerable progress. The African region has nearly 26 million PLWH and accounts for 70% of AIDS-related deaths worldwide; HIV prevalence was estimated at 4.8% in 2014 [7]. It is stable at around 1.2% nationally in Benin [8]. PLWH should benefit from LEAD screening and appropriate care. Higher prevalences of LEAD in PLWH than in the general population have been noted in some studies in sub-Saharan Africa, from 6.9% in Cameroon in 2018 [9] to 18.1% in Burundi in 2021 [10]. In Benin, the only study conducted in 2014 at the National University Hospital of Cotonou showed a high prevalence of LEAD of 35.6% among the 275 PLWH included [11]. There is a lack of recent data on the prevalence of LEAD in PLWH to provide sufficient evidence to guide practice. The objectives of the study were to determine the prevalence of LEAD and to identify the associated factors among PLWH followed at the departmental university hospital center of Ouémé-Plateau in Benin.

2. Methods

2.1. Study Design, Settings, and Population

This was a descriptive and analytical cross-sectional study. It took place in Benin, at the HIV care site for adults in the department of medicine of the target hospital. Testing for HIV and antiretroviral therapy is free. Approximately 1500 patients were followed in 2019. Regarding antiretroviral therapy, combinations of two Nucleoside Reverse Transcriptase Inhibitors (NRTI) and one Integrase Strand Transfer Inhibitor (INSTI) or two Nucleoside Reverse Transcriptase Inhibitors (NRTI) and one Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTI) are recommended in the first line. The main antiretroviral therapies in the first line were Lamivudine (3TC) and tenofovir (TDF) with the combination of Dolutegravir (DTG) or Efavirenz (EFV).

The study population consisted of PLWH followed in the department of medicine of the targeted hospital. Were included, PLWH followed for at least three months, aged at least 25 years, and have given their written consent to participate in the study. PLWH unable to answer questions or with a lower limb amputation, and pregnant women, were excluded.

2.2. Sampling and Data Collection

All PLWH who were monitored during the study period and met the inclusion criteria were successively recruited. Data were collected during a face-to-face interview between the participant and the investigator, followed by the measurement of parameters and the review of the medical record. Sociodemographic, behavioral, and medical information (such as histories of hypertension, diabetes, LEAD, and symptoms of claudication) were collected during the individual interview. Then, the weight, the height, and the blood pressure were measured, following the World Health Organization standards for STEPS surveys [12]. The weight was measured using a mechanical scale and the height was with a portable height rod, brand SECA®. The blood pressure was measured in the left arm of the patient at rest, seated for at least 5 minutes, using an OMRON® brand electronic device. Three measurements were taken at 1-minute intervals after each reading. The average of the last 2 measurements corresponded to the blood pressure value.

ABI was measured by a trained nurse using a SPENGLER manual blood pressure monitor and a vascular Doppler (HUNTLEIGH, model SD2, UK) according to the American Heart Association guidelines [1].

The ABI was calculated separately for each side and corresponded to the ratio between the higher systolic pressure of the ankle and the higher systolic pressure of the arms. The intermittent claudication was researched using the Edinburgh questionnaire [13]. The data were recorded using an electronic form designed with the KoboCollect application.

2.3. Variables Definition

The main variable was LEAD. It was defined by an ABI (right and/or left) ≤ 0.90.

The symptomatic nature of LEAD was defined by the presence of intermittent claudication. The arterial incompressibility was defined by an ABI (right and/or left) ≥ 1.40. The independent variables were defined as follows.

Body mass index (BMI) was calculated by dividing weight in kilograms by height in meters squared. A BMI between 25 kg/m^2 and 30 kg/m^2 was considered overweight, and a BMI ≥ 30 kg/m^2 was an obesity. Abdominal obesity was defined by a waist circumference ≥ 80 cm in women and ≥94 cm in men, according to the criteria of the International Diabetes Federation [14]. Hypertension was defined as the history of hypertension under treatment, or a systolic blood pressure ≥ 140 mm Hg, and/or a diastolic blood pressure ≥ 90 mm Hg during the study.

Behavioral factors were defined according to the criteria of the World Health Organization guidelines [12]. Fruit and vegetable consumption was classified as insufficient if it was less than 5 servings of 80 g (400 g)/day. Physical inactivity corresponded to moderate physical activity (or equivalent) of less than 150 minutes per week.

2.4. Data Analysis

The data were analyzed using the EPI info version 7.2 software. The proportions were calculated for the description of the qualitative variables and the means (with the standard deviation) for the quantitative variables with normal distribution. The proportions of LEAD were compared between the categories of the independent variables using Pearson's chi-square or Fisher's tests.

The identification of the factors associated with LEAD was made through a multivariable analysis following a backward logistic regression. The independent variables were introduced in the model with a significance level of 0.2. Crude and adjusted odds ratios (OR) were calculated. For all comparisons, associations were considered statistically significant if p-value < 0.05.

2.5. Ethical Considerations

The study received the favorable opinion of the educational committee of the School of Public Health of the University of Parakou in Benin. It was conducted with the agreement of the hospital officials. The data was collected and processed confidentially. They were analyzed anonymously.

3. Results

A total of 282 PLWH was monitored during the study period and met the inclusion criteria. Among them, 52 had refused to participate in the study. A response rate was 82%. Out of the 232 PLWH included in this study, 10 had an ABI ≥ 1.40 and were excluded from the data analysis to identify the associated factors of LEAD. The sociodemographic characteristics of 10 PLWH excluded were like those of the study group.

The mean age of the study group (222 PLWH) was 42.9 ± 10.8 years. Soci-

odemographic, behavioral factors and medical histories are detailed in Table 1. The age group "40 years and over" was the most represented (59.5%). There was a female predominance (77.5%). Almost half (45.5%) had no school education. The majority (84.7%) were self-employed. More than half of them had an income below the monthly guaranteed minimum wage of 40,000 FCFA or 80 USD (58.1%) and were married (63.5%).

Table 1. Prevalence of LEAD according to the socio-demographic, economic and behavioral characteristics of the respondents, PLWH study, Departmental University Hospital (Porto-Novo, Benin 2019).

Variables	Sample total n (%) 232 (100)	Sample with ABI < 1.4 n (%) 222 (100)	LEAD (Yes)	
			n (%) 76 (34.2)	p
Age class (years)				0.732
<40	96 (41.4)	90 (40.5)	32 (35.6)	
≥40	136 (58.6)	132 (59.5)	44 (33.3)	
Sex				0.083
Female	179 (77.2)	172 (77.5)	64 (37.2)	
Male	53 (22.8)	50 (22.5)	12 (24.0)	
School education level				0.152
No school education	106 (45.7)	101 (45.5)	35 (34.7)	
Primary	77 (33.2)	74 (33.3)	30 (40.5)	
Secondary or over	49 (21.1)	47 (21.2)	11 (23.4)	
Professional activity				0.119
Independent	196 (84.5)	188 (84.7)	63 (33.5)	
Employed	20 (8.6)	19 (8.5)	10 (52.6)	
Inactive	16 (6.9)	15 (6.8)	3 (20.0)	
Income (FCFA)				0.739
<40,000	134 (57.8)	129 (58.1)	43 (33.3)	
≥40,000	98 (42.2)	93 (41.9)	33 (35.5)	
Marital status				0.888
Single	18 (7.8)	17 (7.6)	7 (41.2)	
Divorce	27 (11.6)	27 (12.2)	8 (29.6)	
Married	149 (64.2)	141 (63.5)	48 (34.0)	
Widower	38 (16.4)	37 (16.7)	13 (35.1)	
Smoking				0.168
Yes	5 (2.2)	5 (2.3)	0 (0)	
No	227 (97.8)	217 (97.8)	76 (35.2)	

Continued

Alcohol intake				0.157
Yes	53 (22.8)	48 (21.6)	12 (25.5)	
No	179 (77.2)	174 (78.4)	64 (36.6)	
Low fruit and vegetable consumption				0.773
Yes	222 (95.7)	212 (95.5)	73 (34.4)	
No	10 (4.3)	10 (4.5)	3 (30.0)	
Physical inactivity				0.975
Yes	50 (21.5)	47 (21.2)	16 (34.0)	
No	182 (78.5)	175 (78.8)	60 (34.3)	
Body mass index (Kg/m²)				
<18.5	8 (3.4)	8 (3.6)	4 (50.0)	0.574
18.5 - 25	140 (60.3)	135 (60.8)	46 (34.1)	
25 - 30	66 (28.5)	63 (28.4)	19 (30.2)	
≥30	18 (7.8)	16 (7.2)	7 (43.8)	
Abdominal obesity				0.227
Yes	77 (33.2)	73 (32.9)	29 (39.7)	
No	155 (66.8)	149 (67.1)	47 (31.5)	
Hypertension				0.020
Yes	66 (28.5)	63 (28.4)	47 (29.6)	
No	176 (71.5)	159 (71.6)	29 (46.0)	
Diabetes				0.301
Yes	4 (1.7)	4 (1.8)	0 (0.0)	
No	228 (98.3)	218 (98.2)	76 (34.2)	

PLWH: People Living With HIV; LEAD: Lower Extremity Artery Disease; ABI; Ankle Brachial Index; p: p-value.

Among them, 2.2% were smokers. Almost a quarter reported physical inactivity (21.2%) and had consumed alcohol in the last 30 days (21.6%). Almost all (95.5%) had an insufficient consumption of fruits and vegetables. There was 7.2% overall obesity, 32.9% abdominal obesity, 28.4% hypertension, and 1.8% diabetes.

Regarding HIV-related characteristics, 89.6% received first-line therapy, 51.3% of patients had a CD4 count greater than 500 cells per mm3, and 10.4% had a detectable viral load ≥ 200 copies per mm3 (Table 2).

The mean left ABI was 0.97 ± 0.14 while the mean right ABI was 0.99 ± 0.13. Out of 222 PLWH, 76 had LEAD, giving a prevalence of 34.2%. For the whole sample ie 232 PLWH, the prevalence was 32.7%. There were no cases of symptomatic LEAD.

Table 2. Prevalence of LEAD according to HIV-related characteristics, PLWH study, Departmental University Hospital (Porto-Novo, Benin, 2019).

Variables	Total Sample n (%) 232 (100)	Sample with ABI < 1.4 n (%) 222 (100)	LEAD (Yes)	
			n (%) 76 (34.2)	p
Antiretroviral therapy				0.017
First line	208 (89.7)	199 (89.6)	63 (31.7)	
Second line	24 (10.3)	23 (10.4)	13 (56.5)	
CD4 count (/mm³)				0.771
<500	117 (50.4)	108 (48.7)	38 (35.2)	
≥ 500	115 (49.6)	114 (51.3)	38 (33.3)	
Viral load (copies/mm³)				0.194
<40	194 (83.6)	186 (83.8)	29 (33.3)	
40 - 200	13 (5.6)	13 (5.8)	7 (53.9)	
≥200	25 (10.8)	23 (10.4)	5 (23.8)	

PLWH: People Living With HIV; LEAD: Lower Extremity Artery Disease; ABI; Ankle Brachial Index; p: p-value.

No significant association was found between the presence of LEAD and sociodemographic factors. The presence of LEAD was significantly associated with hypertension and antiretroviral therapy (Table 3). Hypertensive patients had a higher risk of LEAD compared to non-hypertensive patients (OR = 1.98, 95% CI [1.04 - 3.83], p = 0.037). Those who were on second-line therapy also had a higher risk of LEAD compared to those on first-line therapy (OR = 2.95, 95% CI [1.14 - 7.60], p = 0.025).

4. Discussion

This study showed a high prevalence of LEAD in a sample of PLWH followed at Ouémé-plateau Hospital in Benin with an average age of 42.9 years. The prevalence of LEAD varied according to hypertension status and type of antiretroviral therapy.

The average age of the sample is close to that noted during a study conducted on LEAD prevalence in Burundi among 280 PLWH in 2021 (49.6 years) [10]. It is slightly higher than those observed in two studies in Nigeria in 2018 (43 years) and in Cameroon between 2015 and 2016 (46 years) [9] [15].

Results regarding LEAD prevalence could be compared with other studies conducted in sub-Saharan Africa with LEAD definition based on ABI measurement. However, the cut-off of definition varied in some studies. The prevalence of LEAD is like that noted in 2014 in people living with HIV at the University Hospital of Cotonou (35.6%) [11]. However, it is very high compared to the prevalence reported in previous studies conducted in Cameroon, Nigeria and Burundi from

Table 3. Factors associated of LEAD, PLWH study, Departmental University Hospital (Porto-Novo, Benin, 2019).

Variables	LEAD (Yes)		
	aOR	CI 95%	p
Sex			
Female	1		
Male	0.56	0.26 - 1.22	0.147
School education level			
No school education	1		
Primary	1.47	0.76 - 2.87	0.256
Secondary or over	0.67	0.33 - 1.78	0.535
Professional activity			
Independent	1		
Employed	1.98	0.72 - 5.49	0.188
Inactive	0.90	0.22 - 3.60	0.880
Alcohol intake			
Yes	1		
No	0.69	0.34 - 1.40	0.306
Hypertension			
Yes	1		
No	1.99	1.04 - 3.83	0.037*
Antiretroviral therapy			
First line	1		
Second line	2.95	1.14 - 7.60	0.025*
Viral load (copies/mm^3)			
<40	1		
40 - 200	2.76	0.83 - 9.16	0.097
≥200	0.40	0.13 - 1.26	0.118

PLWH: People Living With HIV; LEAD: Lower Extremity Artery Disease; ABI; Ankle Brachial Index; CI: confidence interval; aOR: adjusted Odd-ratio; p: p-value; *significant $p < 0.05$.

6.9% to 18.1% [9] [10] [15]. It is also higher compared to the data reported in two European studies, in Danish (22.5%) and Polish (4%), [16] [17]. In the general population, several results had been noted in West Africa among adults, especially 12.1% in St Louis (Senegal) in 2012 [18]; 4.7% in Cotonou (Benin) in 2013, and 5.5% in the Tanvè village (Benin) in 2017 [3] [19].

The high prevalence of LEAD in the study can be explained by the differences in the definition of ABI cut-off. In the Cameroon and Nigerian studies among

PLWH, LEAD was defined as ABI < 0.9 while in this study, ABI ≤ 0.9 was used for the diagnosis according to American Heart Association guidelines.

The high prevalence of LEAD can also be linked to the high prevalence of major cardiovascular risk factors such as hypertension and obesity. Indeed, the prevalence of hypertension (28.4%) was higher in the study compared to other African studies (14.2% to 20.9%). In addition, a high prevalence of abdominal obesity (32.9%) was observed. These findings show a combination of cardiovascular risk factors in the targeted PLWH and therefore a high level of overall cardiovascular risk that may partially explain a high prevalence of LEAD.

The type of antiretroviral therapy was associated with LEAD. PLWH treated by second-line antiretroviral therapy had a higher prevalence of LEAD than the others. These results make sense if these patients had a large and prolonged viral load; they were therefore more likely to have LEAD compared to people on first-line therapy. Second-line therapies are prescribed for patients whose treatment has failed under initial treatment. These therapies usually include two nucleoside reverse transcriptase inhibitors and one protease inhibitor. It is possible that these patients had more iatrogenic lipid abnormalities compared to the others. A study in Lomé (Togo) showed that patients on this line of therapy had more dyslipidemia compared to those who received first-line therapy [20]. However, without data on lipid levels, it is difficult to check this hypothesis.

Despite age being a known risk factor of LEAD, no association was observed in the study. Elsewhere, no difference between sexes was noted. Our results are consistent with those reported by Desormais *et al.* in Burundi in 2021 [10].

This study is based on a recommended screening method for LEAD, in particular the measurement of the ABI. Concerning the limitations of the study, the prevalence may be overestimated by errors in recording or reporting ABI values. However, these information biases are negligible since the data was collected by a trained nurse under the supervision of a cardiologist. Measurements were systematically repeated for patients with outliers. Elsewhere, the results could not be generalized to all PLWH in Benin taking into account the recruitment in one center and the convenience sampling. For a representative sample, a multicenter study, including PLWH randomly selected in several sites, is recommended. It will be able to confirm the results and identify other factors associated with LEAD. The temporal sequence cannot be established in our study given the cross-sectional design. Analytical studies, especially prospective cohort studies are more appropriate to establish etiological links.

5. Conclusion

This study showed a high prevalence of LEAD in PLWH included at Ouémé-Plateau Hospital in Benin in 2019. This result is in line with previous data reported in Benin. The associated factors of LEAD were hypertension and type of antiretroviral therapy. Systematic cardiovascular risk assessment and LEAD screening should be integrated into the PLWH care in Benin, especially for hyper-

tensives and those taking second-line antiretroviral therapy. The implementation of a multicenter study will provide representative data. Specific analytical studies will identify other associated factors. All this data will inform the development of recommendations regarding LEAD in PLWH.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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