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Cardiovascular risk factors, global cardiovascular risk, and vascular age in a cohort of Peruvian HIV patients

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Abstract

Introduction: Data on cardiovascular risk and vascular age in patients with human immunodeficiency virus (HIV) from developing countries are scarce. Therefore, the current study aimed to determine the prevalence of cardiovascular risk factors, global cardiovascular risk, and vascular age in a Peruvian cohort of patients with HIV.

Material and methods: A cross-sectional study was conducted among HIV outpatients between August and December 2018. Global cardiovascular risk was calculated using Framingham risk score and ACC/AHA ASCVD score, and vascular age was evaluated using Framingham adaptation.

Results: In total, 310 patients were included. The mean age was 47.4 ± 12.8 years, 79.7% were males, and vascular age was 51.2 ± 17.2 years. The most frequent cardiovascular risk factors were dyslipidemia (69%), hypertension (28.7%), and obesity (18.4%). The median Framingham risk score was 6.15 (range, 3-13) points, and was distributed into low- (67.7%), intermediate- (17.5%), and high- (14.8%) risk. The median ASCVD score was 4.85 (range, 2.4-8) points, and was divided into low- (76.2%), moderate- (13.5%), and high- (10.3%) risk. The prevalence of cardiovascular risk factors was higher in the sub-population aged older than 50 years.

Conclusions: The prevalence of cardiovascular risk factors was high in our cohort of Peruvian patients with HIV. Consequently, overall cardiovascular risk was elevated in > 10% of cases. Vascular age was higher than chronological age.

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Key words: cardiovascular risk, human immunodeficiency virus, vascular age.

Introduction

Cardiovascular disease risk is elevated in patients with human immunodeficiency virus (HIV) infection [1], with multiple contributing factors, e.g., increased prevalence of chronic cardiovascular conditions, such as hypertension, diabetes, dyslipidemia, smoking, and overweight/obesity. In addition, certain antiretroviral drugs have pro-atherogenic

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effects, and the infection is associated with inflammation, immune activation, and microbial translocation [2].

Cardiac and vascular involvement has been observed in HIV-positive patients, even in treatment before antiretroviral combination therapy. These patients have a significantly higher risk of developing atherosclerosis-related cardiovascular events, such as myocardial infarction, cerebrovascular disease, and pulmonary hypertension [3]. A previous study reported that the frequency of HIV patients hospitalized due to vascular cardiac and non-cardiac diseases was one or two cases per year in a national general hospital in Peru [4].

Cardiovascular disease prevention in HIV patients is based on recommendations for non-HIV population, and data on patients from developing countries is lacking. Although international guidelines use different risk models for assessing cardiovascular risks, such as Framingham, SCORE, ASCVD, or DAD methods, there is no specific information on the usefulness of these evaluations in HIV patients [5].

Therefore, this study aimed to determine the cardiovascular risk factors, global cardiovascular risk, and vascular age in a cohort of individuals with HIV from a low-resource setting.

Material and methods

A prospective, cross-sectional study was conducted between August and December 2018. Consecutive adult (age > 18 years) outpatients attending the Hospital Nacional Guillermo Almenara Irigoyen in Lima, Peru, with regular control visits for more than 6 months were included. Electronic medical records of the selected patients were reviewed, and epidemiological, clinical, and laboratory information were collected. No informed consent was required, since all procedures were part of a routine evaluation of patients, and there was no risk for the subjects. All data obtained were handled confidentially.

Dyslipidemia was defined as fasting total cholesterol ≥ 240 mg/dl, and/or fasting triglycerides > 150 mg/dl, and/or low high-density lipoprotein (HDL) cholesterol < 40 mg/dl, and/or high low-density cholesterol (LDL) ≥ 160 mg/dl, or a diagnosis recorded in medical chart. Hypertension was defined as systolic blood pressure ≥ 140 mmHg, diastolic blood pressure ≥ 90 mmHg, or a diagnosis recorded in medical chart or history of taking anti-hypertensive drugs. Diabetes mellitus was described as fasting glucose ≥ 126 mg/dl in two isolated measures, HbA_{1c} ≥ 6.5%, anti-diabetic medicines or insulin utilization, or a diagnosis recorded in medical chart. Smoking was defined as using any form of tobacco product in the previous 30 days, as a matter of habit persistence.

Obesity and overweight were diagnosed with anthropometric data (weight was recorded with a calibrated scale). Obesity was defined as body mass index (BMI) ≥ 30 kg/m^2, and overweight as BMI between 25 and 30 kg/m^2. BMI of each subject was calculated according to standard formula: BMI = weight (kg)/height^2 (m^2). Laboratory tests were performed within 6 months of medical visit and the results were obtained from clinical laboratory's electronic repository. All laboratory examinations were done after at least 10-hour fasting time.

Parameters used for the calculation of risk using the 10-year Framingham risk score, included age, sex, HDL cholesterol level, total cholesterol level, systolic blood pressure, history of hypertension, diabetes, and smoking. On the other hand, parameters used for the calculation of risk using ACC/AHA ASCVD, included age, sex, race, systolic blood pressure, diastolic blood pressure, LDL cholesterol level, HDL cholesterol level, history of diabetes and hypertension, smoking, and statins or aspirin utilization. Vascular age consisted of an adaptation of Framingham risk score described by D'Agostino [5-7].

The 10-year Framingham risk score (FRS) and life-time ACC/AHA ASCVD score were calculated for each participant. The 10-year FRS was categorized as: < 10% low-risk, 10-20% moderate-risk, and ≥ 20% high-risk. For the calculation of ACC/AHA ASCVD score, only individuals aged 40-79 years were considered, and were stratified into low-risk (estimated 10-year risk ≤ 10%), moderate-risk (estimated 10-year risk > 10% and < 20%), and high-risk (estimated 10-year risk ≥ 20%).

Descriptive statistics were applied to summarize epidemiological and clinical findings. Mann-Whitney U and χ^2 tests were applied to assess differences among sub-groups for continuous and categorical variables. Variable age was dichotomized by its mean value. Additionally, an association between some HIV-related factors (time of HIV diagnosis, CDC-3 clinical category, antiretroviral therapy, and virological failure) and cardiovascular risk scores were evaluated using simple linear regression and Mann-Whitney U test, as appropriate. All analyses were performed with R 4.2.0 software, and two-tailed $p < 0.05$ was considered statistically significant.

Results

Three hundred and ten patients were evaluated. Most (80%) were males, the mean age was 47.4 ± 12.8 years, and the median time since HIV diagnosis was 8.3 years (Table 1). Thirty-four percent of patients were in the CDC-3 clinical category, and almost all received antiretroviral therapy. Of them, 13.1% used combined schemes, and 57.5% were based on non-nucleoside reverse transcriptase inhibitors (NNRTI) and protease inhibitors (Table 1).

The most frequent cardiometabolic risk factors were dyslipidemia found in 69% of patients, hypertension in 28.7% (14.6% had a previous diagnosis of hypertension), and obesity in 18.4%. Smoking was reported in 14.5% of cases (80% had a prior smoking history), and 7.7% had diabetes (16.6% had a previous diagnosis of diabetes). Significant differences were observed between the prevalence of hypertension (42.6% vs. 17.2%) in patients aged ≥ 50 years compared with patients aged < 50 years as well as an increasing prevalence of diabetes (11.3% vs. 4.7%) between these groups. Differences between cardiovascular comorbidities, gender, stage of infection (CDC-3 vs. non-CDC-3), or treatment results (viral suppression vs. virological failure) were not found (Table 2).

Table 1. Clinical and demographic characteristics of the selected population

Parameters	Data
Age (years), mean ± SD	47.4 ± 12.8
Males, *n* (%)	247 (79.7)
Median time of HIV diagnosis (months), (IQR)	99.5 (48-204)
C3 clinical stage, *n* (%)	105 (33.9)
Antiretroviral therapy, *n* (%)	306 (98.7)
Based on NNRTI	127 (41.5)
Based on PI	49 (16.0)
Based on integrase inhibitors	90 (29.4)
Combined schemes	40 (13.1)
Viral suppression, *n* (%)	294 (94.8)
Virological failure, *n* (%)	16 (5.2)

HIV – human immunodeficiency virus, IQR – interquartile range, NNRTI – non-nucleoside reverse transcriptase inhibitors, PI – protease inhibitors, SD – standard deviation

The mean vascular age was 51.2 ± 17.2 years, a higher value than the chronological age. In individuals aged < 50 years, the median difference between vascular and chronological age was 3 (95% CI: –3-9%) years. 30.6% of patients had values lower than the chronological age, 2.1% had the same value as the chronological age, and 67.3% had a higher vascular age. In individuals aged ≥ 50 years, 38.5% had values lower than the chronological age, 4.7% had the same value as the chronological age, and 56.8% had a higher vascular age (Table 3).

Cardiovascular risk was categorized according to the Framingham risk score. The median value of the total risk was 6.15 (range, 3-13) points. Of the total cohort, 210 (67.7%) had low-risk, 54 (17.5%) had moderate-risk, and 46 (14.8%) presented high-risk. For individuals aged between 40 and 79 years (n = 214), the median value of ACC/AHA ASCVD score was 4.85 (range, 2.4-8) points. According to the punctuation, 163 (76.2%) had low-risk, 29 (13.5%) had moderate-risk, and 22 (10.3%) had a high-risk. The frequency of cardiovascular risk factors and the prevalence of Framingham global cardiovascular risk were compared with other Peruvian studies published (Table 4) [8-15]. Only the time of HIV diagnosis was significantly associated with cardiovascular risk score (Table 5).

Discussion

In this sample of HIV-infected adults treated with antiretroviral therapy, predominantly with NNRTI-based drugs and regimens based on protease inhibitors, we found a high proportion of cardiovascular risk factors compared with that previously reported in our country's HIV and general populations [8, 15]. The sample corresponds to 20% of patients treated in the hospital during the study period.

Table 2. Metabolic and cardiovascular comorbidities in the total population and differences between age groups

Comorbidities	Total population, *n* (%)	< 50 years	≥ 50 years
Dyslipidemia	214 (69.0)	65.7%	73.4%
Diabetes	24 (7.7)	4.7%*	11.3%*
Hypertension	89 (28.7)	17.2%*	42.6%*
Smoking	45 (14.5)	15.4%	13.5%
Obesity	57 (18.4)	18.3%	19.1%

**χ^2 test, p-value < 0.05*

Table 3. Differences in vascular age and chronological age (< 50 years vs. ≥ 50 years)

Parameters	Total population	< 50 years	≥ 50 years
Variation in years, median (IQR)	3 (–3-9)	2 (–4-7)*	6 (15)*
Below chronological age			
Less than over 10 years	3.5%	4.3%	2.9%
Less than 5-10 years	13.2%	7.8%	17.8%
Less than 5 years	18.0%	18.5%	17.8%
Equal chronological age	3.5%	2.1%	4.7%
More than chronological age			
More than 0-5 years	19.4%	13.4%	24.3%
More than 5-10 years	19.4%	18.5%	20.2%
More than 10-20 years	15.5%	23.4%	8.8%
More than 20-30 years	6.5%	10.6%	2.9%
More than 30 years	1.0%	1.4%	0.6%

*IQR – interquartile range; *χ^2 test, p-value = 0.001*

The predominance of male participants reflects local epidemiology of HIV infection, with a discrete predominance of patients aged over 50 years. The cut-point of 50 years of age was selected according to the mean age of total population. In our cohort, dyslipidemia was the most common cardiovascular risk factor. The onset of HIV infection is associated with a decreased total cholesterol, LDL-C, and HDL-C levels. The effect of antiretroviral therapy on lipid levels varies significantly among classes of antiretroviral drugs and even among medications within the same class. According to previous literature, NNRTIs (mainly based on lopinavir boosted with ritonavir) and PIs (mainly based on efavirenz) were associated to mixed dyslipidemia and hypertriglyceridemia [6, 16].

Table 4. Comparison of cardiovascular risk factors and global cardiovascular risk in Peruvian HIV-positive patients

Characteristics	Valenzuela *et al.*, 2024 (*n* = 310)	Hidalgo *et al.*, 2018 (*n* = 305) [8]	Valencia *et al.*, 2008 (*n* = 36) [9]	Cahn *et al.*, 2009 (*n* = 417) [10]	Lister *et al.*, 2013 (*n* = 111) [11]	Valenzuela *et al.*, 2006 (*n* = 276) [12]	Rondan *et al.*, 2017 (*n* = 538) [13]	Peruvian population studies [14, 15]
Age (years), mean/median	47.4	46	NR	39.1	47.0	NR	40	NR
Males	79.7%	73.1%	NR	70.7%		73.18%	73.2%	NR
Dyslipidemia	69.0%	51.5%	NR	67.9%	76.6%	34.05%	74.7%	37.9%
Diabetes	7.7%	7.2%	NR	1.7%	1.8%	1.81%	NR	7.0%
Obesity	18.4%	11.1%	NR	6.5%	NR	4.71%	NR	14.3%
Hypertension	28.7%	8.85%	NR	14.6%	NR	3.26%	NR	27.3%
Smoking	14.5%	NR	NR	15.6%	18.0%	3.96%	NR	23.2%
High Framingham-risk score	14.8%	NR	NR	NR	3.6%	2.89%	NR	NR

NR – not reported

Overall, the prevalence of dyslipidemia among people living with HIV across various studies ranges from 28% to 80%, with hypertriglyceridemia being the most common abnormality [16] (Table 4).

The prevalence of diabetes and hypertension was higher in individuals aged over 50 years, reflecting a severe vascular compromise. HIV infection is correlated with an increased risk of insulin resistance, and antiretroviral therapy is associated with an increased risk of insulin resistance, metabolic derangement, and type 2 diabetes occurrence. Likewise, tuberculosis and viral hepatitis co-infections are highly prevalent among patients with HIV infection and, independently, are associated with an increased risk of diabetes [17].

Hypertension is a significant risk factor in cardiovascular disease, and its prevalence is higher in the HIV population, despite viral suppression by antiretroviral therapy. Its prevalence ranges between 4% to 54% by population and sub-groups, even within the same countries. Its pathogenesis emerges from three main factors: HIV-related inflammation, HIV-related proteins (i.e., NeF, TaT, and gp-120), and genetic predisposition [18].

Some recent investigations have reported a higher prevalence of clinical and sub-clinical cardiovascular disease in HIV-infected adults associated with poorer immune control and traditional cardiovascular risk factors, such as diabetes, hypertension, dyslipidemia, and smoking, which generate chronic inflammation, endothelial damage, and atherosclerosis [6].

It is important to emphasize that the prevalence of cardiovascular risk factors was higher in our cohort of HIV-infected adults compared with the prevalence of them among the total Peruvian population, with significant differences in dyslipidemia (69% vs. 37.9%).

Cardiovascular risk assessment must be considered in all HIV-infected adults. A few clinical scores have been developed for HIV population (DAD and HIV-CARDIO-PREDICT), but scores for general population can be employed (ACC/AHA PCE-ASCVD, FHS-CVD, SCORE 2, SCORE 2-OP, SMART, and ADVANCE). Moreover, various validated tests and new biomarkers can identify persons with early atherosclerosis and cardiovascular disease [7, 19].

Ten and fourteen percent of our cohort had a higher cardiovascular risk according to the ACC/AHA ASCVD score and the Framingham risk score. The applicability of cardiovascular risk prediction tools developed for the general population is unclear for the HIV-infected population, although every instrument can be helpful as a preventive approach. In our study, more patients were classified as high-risk according to the Framingham risk score, which differs from other international cohort studies, where ASCVD score can classify more patients with elevated cardiovascular risk than in our population [20]. Therefore, we propose that every risk score can help identify a group of patients that need close follow-up and early preventive/therapeutic interventions.

The concept of vascular age (also known as heart age) was first introduced in 2008 by D'Agostino, and presents the hypothetical age of vascular system of a patient with

Table 5. Factors associated with cardiovascular risk scores in Peruvian HIV-positive patients

Factors	10-year Framingham risk score		Life-time ACC/AHA ASCVD score	
		p-value		*p*-value
Time of HIV diagnosis (months)*	0.028 (0.011-0.045)	0.001	0.015 (0.003-0.026)	0.010
C3 clinical stage**				
Yes	6.6 (2.8-12.2)	0.595***	5 (2.4-7.4)	0.915***
No	6.1 (3.3-13.4)		4.8 (2.3-8.1)	
Antiretroviral therapy**				
Yes	6.25 (3.0-13.2)	0.253***	4.8 (2.3-8.0)	0.177***
No	3.8 (1.3-8.6)		7.7 (5.5-12.2)	
Virological failure**				
Yes	4.75 (2.25-13.4)	0.859***	5.1 (1.9-7.6)	0.977***
No	6.25 (3.0-12.5)		4.8 (2.4-8.0)	

**Beta coefficient (95% CI) from simple linear regression. **Median (interquartile range). ***Mann-Whitney U test.*

cardiovascular risk factors compared with the chronological age of a subject. The information related to vascular age (as the age of arteries), is a concept related to the risk that all patients might more easily understand, because it is quantitative data. Moreover, it may help the physician explain the patient's risk status and improve patient adherence with preventive measures or therapeutic interventions [21-25]. Reports describing variations of vascular age in the HIV population are scarce. In the current study, a difference of 4 years between vascular and chronological age was observed, with a median of 6 years in the higher age sub-population. In a previous study on vascular age in a population of 1,432 HIV-positive men, the median vascular age eclipsed the chronological median age between 9 and 13 years [23].

It is well-known that there are disparities in the quality of cardiovascular care between HIV-infected versus non-HIV-infected adults in the United States [24]. A similar situation can occur in some Latino-American countries. To surpass this situation, we suggest including cardiovascular risk assessment and recommendations for managing cardiovascular risk factors in the HIV guidelines of every nation.

Our study has some limitations. First, there is a lack of a control group, as we primarily focused on the description of cardiovascular risk factors, cardiovascular risk scores, and vascular age for the whole sample and comparison by age category. Second, laboratory results were collected at a different time than physical and anthropometric evaluation. However, the obtained data is the most recently published information in Peru that includes quantifying cardiovascular risk and vascular age calculation. The latter has not been well-described for the HIV population. Finally, the sample size of our study was limited.

Conclusions

We observed a high prevalence of cardiovascular risk factors in a cohort of Peruvian HIV-positive patients. The global cardiovascular risk was found increased in > 10% of the patients using the Framingham Risk and ASCVD scores. Furthermore, the vascular age was higher than the chronological age. Nevertheless, more studies are needed to address the long-term cardiovascular complications in this population.

Disclosures

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2. Assistance with the article: None.
3. Financial support and sponsorship: None.
4. Conflict of interests: None.

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