Original Article

Quantification of subclinical plaque characteristics and perivascular fat using coronary computed tomography angiography (CCTA) among individuals with human immunodeficiency virus (HIV)

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Background: People infected with human immunodeficiency virus (PIWH) have a higher risk of cardiovascular events. This study was designed to compare the differences in plaque characteristics and perivascular fat between subclinical coronary atherosclerosis in PIWH and healthy controls (HC) by coronary computed tomography angiography (CCTA). We also assessed the associations between human immunodeficiency virus (HIV) infection, antiretroviral therapy (ART), and coronary artery disease (CAD).

Methods: This cross-sectional study included a total of 158 PIWH and 79 controls. CCTA was used to evaluate coronary artery plaque prevalence, coronary stenosis severity, plaque composition, plaque volume, and perivascular fat attenuation index (FAI). Logistic regression analyses were used to assess the associations between the prevalence of coronary artery plaque and HIV-related clinical indicators.

Results: There was no difference in total coronary artery plaque prevalence between PIWH and controls (44.3% *vs.* 32.9%; P=0.09), but the prevalence of noncalcified plaque was significantly higher in PIWH compared with the controls (33.5% *vs.* 16.5%; P=0.006). After adjustment for age, sex, statin use, and family history of cardiovascular disease (CVD), the prevalence of noncalcified plaque remained 2 times higher in PIWH [odds ratio (OR), 2.082; 95% confidence interval (CI): 1.007–4.304; P=0.048]. The perivascular FAI measured around the left anterior descending artery (LAD) was higher in PIWH (–71.4±5.7 *vs.* –73.5±7.0;

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P=0.03) compared with that of the controls. The intra-group analyses of PIWH suggested that the decrease in nadir CD4+ T-cell count was associated with the increased prevalence of noncalcified plaque (OR, 4.139; 95% CI: 1.312–13.060; P=0.02).

Conclusions: PIWH have a higher risk of developing noncalcified plaque and greater perivascular fat. In addition, the increased noncalcified plaque prevalence in PIWH may be associated with the immunodeficiency caused by HIV.

Keywords: Human immunodeficiency virus (HIV); antiretroviral therapy (ART); coronary computed tomography angiography (CCTA); subclinical coronary atherosclerosis; perivascular fat

Submitted Jan 15, 2024. Accepted for publication May 14, 2024. Published online Jun 13, 2024.
doi: 10.21037/qims-24-79
View this article at: https://dx.doi.org/10.21037/qims-24-79

Introduction

With the development and application of antiretroviral therapy (ART), people infected with human immunodeficiency virus (PIWH) now have a higher life expectancy, and acquired immune deficiency syndrome (AIDS) has now become a chronic disease (1). Non-AIDS-related death has become the leading cause of death in most PIWH, of which coronary artery disease (CAD) is the main cause (2). Previous foreign studies suggested a higher risk ratio of cardiovascular events varying from 1.5 to 2.1 in PIWH compared with the general population (3-5). The reasons for the high prevalence of CAD in PIWH are complex and still inconclusive, and may be associated with multiple factors such as adverse viral effects on endothelial cells, pro-coagulant and pro-inflammatory mechanisms in the setting of immunosuppression, adverse metabolic effects of certain ART agents including insulin resistance and dyslipidemia, and traditional cardiovascular risk factors (6-8).

There has been considerable interest in the early diagnosis of subclinical atherosclerosis in PIWH. Coronary computed tomography angiography (CCTA) is a noninvasive imaging method that can assess coronary stenosis severity and the type of plaque. Perivascular fat is a special visceral adipose tissue (9-12) that can promote inflammation and atherosclerosis by secreting active mediators through the paracrine pathway (13,14). Changes in perivascular fat attenuation index (FAI) values obtained by computer post-processing techniques can be used to quantify coronary artery inflammation and provide imaging evidence for risk stratification of coronary atherosclerosis (15,16).

Previous studies have mostly focused on the general population (17-19), and although there have been some studies on subclinical CAD in PIWH, the results have been inconsistent (20-24). The differences in race, living habits, treatment, drug exposure, and traditional cardiovascular risk factors in PIWH may lead to differences in results. At present, there are few studies about coronary human immunodeficiency virus (HIV)-related atherosclerosis in Chinese PIWH.

Thus, this study aimed to characterize coronary atherosclerosis and explore related factors using CCTA in a Chinese cohort of PIWH. We present this article in accordance with the STROBE reporting checklist (available at https://qims.amegroups.com/article/view/10.21037/qims-24-79/rc).

Methods

Study population

In this cross-sectional study, we recruited 170 PIWH and 85 healthy controls (HC) from the AIDS Laboratory in The First Hospital of China Medical University between December 2019 and June 2021. The inclusion criteria for PIWH were as follows: (I) diagnosis of HIV infection, (II) age between 30 and 70 years, and (III) under ART. The exclusion criteria for PIWH were as follows: (I) previous history of CAD or symptoms such as angina, (II) contraindications of CCTA examination, (III) inadequate image quality, and (IV) incomplete clinical data. HC who were matched according to age were recruited. The inclusion criteria for HC were normal health without signs of cardiovascular diseases (CVDs), and normal electrocardiogram examination. After exclusion, our study eventually included 158 PIWH and 79 controls (see flowchart in *Figure 1*).

We collected the data of age, sex, body mass index

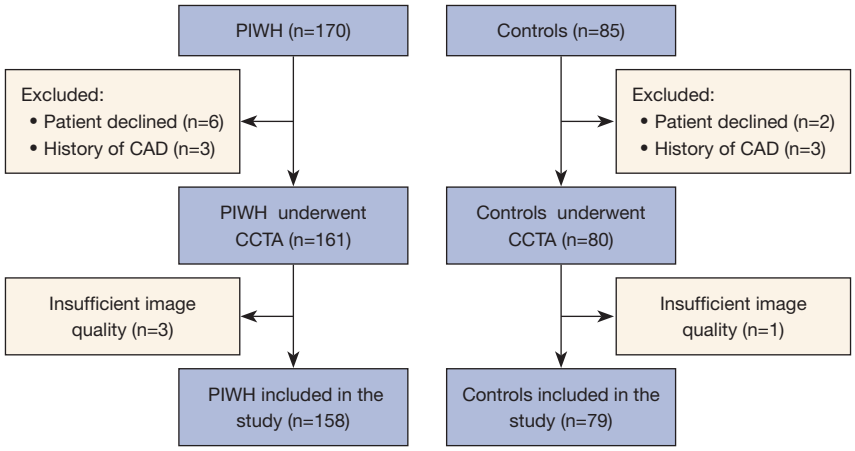

Figure 1 Participant flowchart. PIWH, people infected with human immunodeficiency virus; CAD, coronary artery disease; CCTA, coronary computed tomography angiography.

(BMI), traditional cardiovascular risk factors, and statin use of all participants. Traditional cardiovascular risk factors included smoking, dyslipidemia, diabetes, hypertension, and family history of CVD. Diabetes was defined as fasting serum glucose >7.0 mmol/L. Hypertension was defined based on resting systolic blood pressure (SBP) values 140 mmHg and/or diastolic blood pressure (DBP) 90 mmHg. We also collected the CD4+ T-cell count (current count and nadir count), CD8+ T-cell count, viral load, time of HIV diagnosis, time of ART use, and ART regimens of PIWH. Detectable viral load was defined as ≥50 copies/mL. The ART drugs used mainly included nucleoside reverse transcription inhibitor (NRTI), non-nucleoside reverse transcription inhibitor (NNRTI), and protease inhibitor (PI). The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Board of The First Hospital of China Medical University (No. 2019-228-2) and informed consent was provided by all participants.

Image acquisition

CCTA was carried out using a SOMATOM 128-slice dual-source computed tomography (CT) scanner (Definition; Siemens Medical Solutions, Forchheim, Germany) and 50–60 mL intravenous contrast (iopamidol, 370 mg/mL, Brocco Si, Shanghai, China) at a flow rate of 4–5 mL/sec. The scan parameters were as follows: tube voltage =120 kV, automatic tube current modulation (reference tube current 300–400 mAs), slice thickness =0.75 mm, detector collimation =2×64×0.6 mm, and matrix =512×512. All participants used retrospective electrocardiographic gating with a heart rate of 50–100 beats per minute.

Image post-processing

All images were analyzed using cardiovascular post-processing software (Syngo.via version VB20; Siemens Healthineers, Forchheim, Germany). Image analyses were carried out by 2 independent observers with more than 5 years' experience in cardiovascular imaging. In case of disagreement, a consensus was obtained after consultation.

Coronary plaque analysis

On non-contrast CT images, coronary artery calcium (CAC) score measurement was carried out using the method of Agatston (25). On CCTA images, coronary plaques were classified as calcified and noncalcified by 2 independent observers. Calcified and noncalcified plaque were defined as CT values ≥150 Hounsfield units (HU) and <150 HU, respectively. According to Coronary Artery Disease Reporting and Data System (CAD-RADS), the severity of coronary stenosis was quantified and divided into 6 categories: 0% = no visible stenosis, <25% = minimal stenosis, 25–49% = mild stenosis, 50–69% = moderate stenosis, 70–99% = severe stenosis, and 100% = occluded (26). We assessed coronary artery stenosis in general, that is, the presence of one or more coronary lesions causing vessel stenosis greater than 50% or 70%.

The software allows semiautomatic, quantitative assessment of the composition and volume of plaques. The

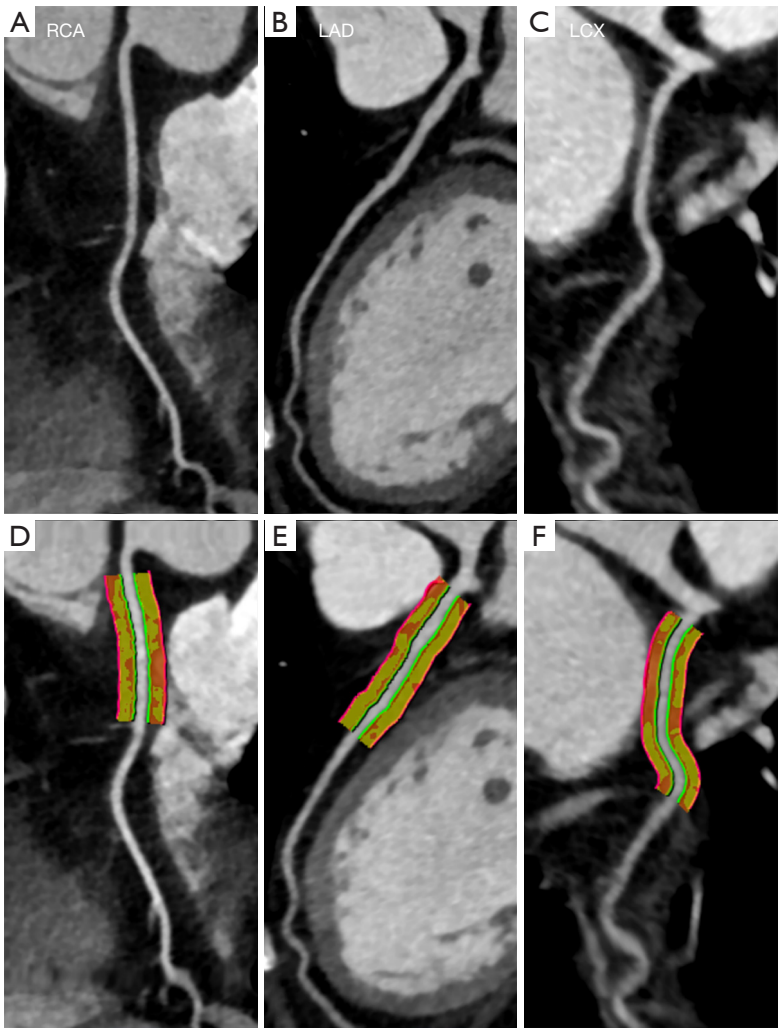

Figure 2 Measurement of the perivascular FAI of the 3 major coronary arteries. (A-C) The original images of the RCA, LAD and LCX. (D) The perivascular FAI of the RCA was measured 10 mm from the opening of the RCA. (E,F) The perivascular FAI of the LAD and LCX was measured from the opening of the LM. RCA, right coronary artery; LAD, left anterior descending artery; LCX, left circumflex artery; FAI, fat attenuation index; LM, left main coronary artery.

proximal and distal boundaries of the plaque were manually segmented, and the software would automatically outline the inner and outer walls of the vessels. Plaque delimitation was adjusted manually when inaccurate. Plaque composition was assessed using attenuation-stratified measurements, with the definition as follows: low attenuation, <30 HU; intermediate attenuation, 31–130 HU; and high attenuation, >131 HU (27).

Perivascular fat analysis

Perivascular fat was defined as the adipose tissue voxels located within a distance from the perimeter of the vessel equal to the diameter of the vessel (14). CT attenuation thresholds between –190 and –30 HU were used to identify the perivascular fat (14). The FAI of the 3 major coronary arteries was measured by software, including left anterior descending artery (LAD), left circumflex artery (LCX), and the right coronary artery (RCA). The measuring length was 40 mm. The perivascular FAI of the RCA was measured 10 mm from the opening of the RCA to avoid the effect of the aortic root (15). The perivascular FAI of the LAD and LCX was measured from the opening of the left main coronary artery (*Figure 2A-2F*).

Statistical analysis

Continuous variables were expressed as mean ± standard deviation (SD) or median with 25th–75th percentile interquartile range (IQR) after normality test. Categorical variables were expressed as numbers and percentages. Continuous variables were analyzed using a Mann-Whitney U test or *t*-tests when suitable. Chi-squared test or Fisher's exact test was used for categorical variables, as appropriate.

Binary logistic regression analysis was used to evaluate the associations between HIV-related clinical indicators and the prevalence of plaque in HIV-infected participants. Age, sex, statin use, and family history of CVD were adjusted in multivariable analyses. A 2-tailed P value <0.05 was considered statistically significant.

All statistical analyses were carried out using SPSS software (V26.0; IBM Corp., Armonk, NY, USA).

Results

Clinical characteristics

A total of 237 participants (158 PIWH and 79 HC) were enrolled in this study, all of whom underwent both CAC determination and CCTA. PIWH had a median age of 52 (IQR 45–57) years, whereas controls had a median age of 51 (IQR 45–59) years. Compared with controls, PIWH were predominantly male [85.4% (135/158) *vs.* 73.4% (58/79), respectively; P=0.03]. The median BMI of PIWH was lower than that of controls [23.1 (21.8–25.7) *vs.* 25.4 (22.6–27.20); P<0.001]. There was no significant difference in age, statin use and traditional cardiovascular risk factors, including smoking, hypertension, diabetes, family history of CVD, and dyslipidemia (all P>0.05).

In PIWH, the median time of HIV diagnosis was 7 (IQR 4–10) years, and all were undergoing ART. The median time of ART use was 6 (IQR 3–9) years. Among 158 participants, 11 had detectable viral load. Almost all of them used NRTI, 69.6% of patients were on NNRTI-based regimen, 8.9% of patients were on a PI-based regimen, and 20.9% of patients used other ART drugs (see *Table 1*). The median current CD4+ T-cell count was 566 (IQR 435–734) cells/mm^3, and the median nadir CD4+ T-cell count was 266 (IQR 164–367) cells/mm^3 (*Table 2*).

Imaging results

In CCTA results, coronary artery plaque prevalence was 44.3% and 32.9% in PIWH and HC, respectively (P=0.09). The prevalence of a coronary artery stenosis severity higher than 50% was 12.0% in PIWH and 3.8% in HC (P=0.07). The prevalence of coronary artery stenosis severity of more than 70% was 2.5% in PIWH and 0% in HC. The perivascular FAI of the LAD was higher in PIWH compared with controls (−71.4±5.7 *vs.* −73.5±7.0 HU; P=0.03). However, there were no significant differences in the perivascular FAI of the RCA and LCX between the 2 groups (all P>0.05, see *Table 3*).

After stratification by plaque types, the prevalence of noncalcified plaque was significantly higher in PIWH compared with the HC (33.5% *vs.* 16.5%; P=0.006) (*Figure 3*). Univariable analyses suggested that HIV infection, age, and family history of CVD were risk factors for the prevalence of noncalcified plaque. In multivariable analysis, after adjustment for age, sex, statin use, and family history of CVD, the prevalence of noncalcified plaque remained two times higher in PIWH [odds ratio (OR), 2.082; 95% confidence interval (CI): 1.007–4.304; P=0.048] (*Figure 4*).

In participants with plaque present, median CAC score was 18.2 (IQR 0.4–97.6) in PIWH and 17.2 (IQR 1.4–53.5) in HC (P=0.76). The median total plaque volume was larger in PIWH than in HC [146.1 (67.9–263.7) *vs.* 90.7 (42.5–120.6); P=0.009]. After stratification by plaque composition, intermediate-attenuation plaque volume was larger in PIWH than in HC [84.5 (45.6–183.6) *vs.* 55.7 (25.6–74.5); P=0.007] (*Table 3*).

Associations between plaque prevalence and HIV-related clinical indicators

The associations between plaque prevalence and HIV-related clinical indicators were evaluated in 158 PIWH. The results indicated that current CD4+ T-cell count, nadir CD4+ T-cell count, CD4+/CD8+ ratio, time of HIV diagnosis, time of ART use, and ART regimens were not associated with total plaque prevalence and calcified plaque prevalence.

However, the decrease in nadir CD4+ T-cell count was associated with the increased prevalence of noncalcified plaque. In the univariable analyses, the prevalence of noncalcified plaque in PIWH with nadir CD4+ T-cell count less than 100 was 4.407 times higher than that in PIWH with CD4+ T-cell count greater than 350 (OR, 4.407; 95% CI: 1.519–12.786; P=0.006) (Table S1). After adjustment for age, sex, statin use, and family history of CVD, a difference still existed (OR, 4.139; 95% CI:

Table 1 Clinical characteristics of participants

Variables	PIWH (n=158)	HC (n=79)	P value
Age (years)	52 (45–57)	51 (45–59)	0.76
Male sex	135 (85.4)	58 (73.4)	0.03*
BMI (kg/m^2)	23.1 (21.8–25.7)	25.4 (22.6–27.2)	<0.001*
Heart rate (bpm)	69 (60–82)	68 (61–77)	0.59
Cardiovascular risk factors			
Smoking	46 (29.1)	20 (25.3)	0.54
Hypertension	23 (14.6)	16 (20.3)	0.27
Diabetes	6 (3.8)	7 (8.9)	0.11
Family history of CVD	32 (20.3)	9 (11.4)	0.09
Dyslipidemia	93 (58.9)	47 (59.5)	0.93
Total cholesterol (mmol/L)	4.7 (4.2–5.3)	5.1 (4.2–5.6)	0.13
Triglycerides (mmol/L)	1.7 (1.0–2.8)	1.5 (1.0–2.8)	0.61
HDL cholesterol (mmol/L)	1.2 (1.0–1.4)	1.2 (1.0–1.4)	0.77
LDL cholesterol (mmol/L)	2.9 (2.4–3.5)	3.2 (2.5–3.7)	0.14
Statin	14 (8.9)	11 (13.9)	0.23
Time of HIV diagnosis (years)	7 (4–10)	–	–
Time of ART use (years)	6 (3–9)	–	–
ART regimens			
2 NRTI + 1 NNRTI	110 (69.6)	–	–
2 NRTI + 1 PI	14 (8.9)	–	–
Others	33 (20.9)	–	–
Detectable viral load	11 (7.0)	–	–
CD4 current (cell/mm^3)	566 (435–734)	–	–
CD4 nadir (cell/mm^3)	266 (164–367)	–	–
CD8 current (cell/mm^3)	793 (574–1,090)	–	–
CD4/CD8	0.7 (0.5–1.1)	–	–

Data are expressed as n (%) or median (IQR). *, P<0.05. PIWH, people infected with human immunodeficiency virus; HC, healthy controls; BMI, body mass index; CVD, cardiovascular disease; HDL, high-density lipoprotein; LDL, low-density lipoprotein; HIV, human immunodeficiency virus; ART, antiretroviral therapy; NTRI, nucleoside reverse transcriptase inhibitor; NNTRI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; IQR, interquartile range.

1.312–13.060; P=0.02) (*Table 4*).

Discussion

To our knowledge, this is the first large-sample study in China, and the results are of great significance for the early diagnosis and intervention of CAD in PIWH. The main findings of this study are as follows: (I) the prevalence of noncalcified plaque in Chinese PIWH was significantly higher than in HC, but there were no differences in the prevalence of total and calcified coronary artery plaque. (II) The perivascular FAI of the LAD was higher in PIWH compared with HC, but no difference in perivascular FAI of the RCA and LCX was found. (III) The intra-group

Table 2 HIV-related clinical variables

Variables	PIWH (n=158)
CD4 current (cells/mm^3)	566 (435–734)
<350	18 (11.4)
350–700	94 (59.5)
>700	46 (29.1)
CD4 nadir (cells/mm^3)	266 (164–367)
<100	26 (16.5)
100–199	30 (19.0)
200–350	59 (37.3)
>350	43 (27.2)
CD8 current (cells/mm^3)	793 (574–1,090)
CD4/CD8	0.7 (0.5–1.1)
<0.5	45 (28.5)
0.5–1.0	66 (41.8)
>1.0	47 (29.7)
Time of HIV diagnosis (years)	7 (4–10)
<5	48 (30.4)
5–10	66 (41.8)
>10	44 (27.8)
Time of ART use (years)	6 (3–9)
<5	56 (35.4)
5–10	75 (47.5)
>10	27 (17.1)

Nonnormally distributed variables were expressed as medians (25th–75th percentile IQR). Categorical variables are expressed as number (percentage). PIWH, people infected with human immunodeficiency virus; HIV, human immunodeficiency virus; ART, antiretroviral therapy; IQR, interquartile range.

analyses of PIWH suggested that the decrease in nadir CD4+ T-cell count was associated with the increased prevalence of noncalcified plaque, even after adjustment for age, sex, statin use, and family history of CVD.

Previous studies from Canada and Austria have suggested that PIWH have a higher prevalence of noncalcified plaque than HC with similar traditional cardiovascular risk factors (22,28), which is similar to our findings. We know that calcified plaque may reflect more advanced but stable atherosclerosis, whereas noncalcified plaque may appear earlier and may be more prone to rupture. A meta-analysis of the general population suggested that noncalcified plaques are strong predictors of adverse cardiovascular events as compared with calcified plaques (29). Therefore, early identification of the occurrence of noncalcified plaques through CCTA may help to stratify the risk of cardiovascular events in PIWH. In contrast to our study, a Swiss cohort study found that PIWH and HC had a similar prevalence of noncalcified plaque and high-risk plaque, whereas the prevalence of calcified plaque in PIWH was relatively lower (21). This may be associated with regular follow-up and high rates of successful treatment of PIWH in that cohort. A study of African Americans suggested that the correlation between subclinical coronary atherosclerosis and HIV infection was inconclusive but independently associated with cocaine use (30). Therefore, differences in results may be caused by differences in race, HIV infection duration, and ART.

Perivascular fat secretes a large amount of pro-inflammatory, pro-atherosclerotic adipokines through morphological and functional changes, thus promoting plaque progression and changes in plaque phenotype (13,14). Even with ART, immune activation and inflammation were generally higher in PIWH than in people without infection. In our study, the perivascular FAI of the LAD was higher in PIWH compared with HC, possibly affecting the physiological function and pathophysiological processes of the coronary arteries by coronary inflammation. First, there are anatomical differences between the 3 coronary arteries. Second, previous studies have shown that atherosclerosis occurs mainly and earlier in LAD among the 3 coronary arteries (31). Different coronary arteries have different plaque progression: LAD has a higher plaque and calcium deposit burden than RCA and LCX (32). The different environments for the development of atherosclerotic plaques may contribute to differences in the risk of acute coronary events among different coronary arteries. In addition, the FAI around the LAD demonstrated the highest correlation with the FAI around culprit lesions in patients with acute coronary syndrome (ACS), which could be used to represent whole heart inflammation and could improve the identification of patients with ACS and stable CAD (33). Therefore, this study has presented that perivascular FAI measures may be an important imaging biomarker for tracking asymptomatic CVD progression in PIWH (34). Quantification of perivascular fat can evaluate the relationship between perivascular fat and HIV-related factors, and it may play an important role in the development of CAD in subclinical PIWH (35).

Table 3 Imaging results of participants

Variables	PIWH (n=158)	Controls (n=79)	P value
Total plaque prevalence	70 (44.3)	26 (32.9)	0.09
Calcified plaque prevalence	41 (25.9)	17 (21.5)	0.46
Noncalcified plaque prevalence	53 (33.5)	13 (16.5)	0.006*
Coronary artery stenosis >50%	19 (12.0)	3 (3.8)	0.07
Coronary artery stenosis >70%	4 (2.5)	0 (0)	–
RCA-FAI (HU)	−70.3±6.7	−71.9±7.1	0.09
LAD-FAI (HU)	−71.4±5.7	−73.5±7.0	0.03*
LCX-FAI (HU)	−67.4±5.5	−66.9±5.6	0.48
CAC score	18.2 (0.4-97.6)	17.2 (1.4–53.5)	0.76
Total plaque volume (mm^3)[a]	146.1 (67.9–263.7)	90.7 (42.5–120.6)	0.009*
Low-attenuation plaque volume (mm^3)[a]	4.6 (0.7–17.5)	6.0 (0.6–12.0)	0.47
Intermediate-attenuation plaque volume (mm^3)[a]	84.5 (45.6–183.6)	55.7 (25.6–74.5)	0.007*
High-attenuation plaque volume (mm^3)[a]	18.9 (10.3–72.8)	10.5 (4.8–55.0)	0.50

Data were expressed as mean ± SD, n (%), or median (IQR). *, P<0.05. [a], in participants with plaque present. PIWH, people infected with human immunodeficiency virus; RCA, right coronary artery; FAI, fat attenuation index; HU, Hounsfield units; LAD, left anterior descending branch; LCX, left circumflex coronary artery; CAC, coronary artery calcium; SD, standard deviation; IQR, interquartile range.

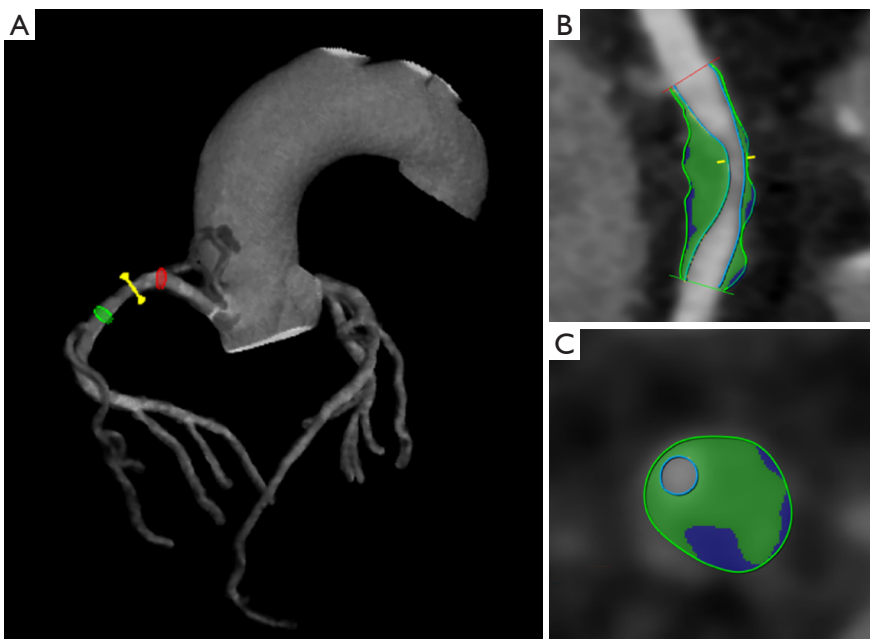

Figure 3 A 60-year-old man infected with HIV. The reconstruction images of CCTA display a noncalcified plaque in the RCA, with lumen stenosis of more than 70% and a plaque volume of 317.98 mm^3. (A,B) The red line marks the proximal end of the plaque; the green line marks the distal end of the plaque; and the yellow line marks the minimum luminal area, where the stenosis is maximum. (C) Cross-sectional image of the plaque at the position indicated by the yellow line in (B). Green indicates intermediate-attenuation plaque (31–130 HU). Blue indicates low-attenuation plaque (<30 HU). HIV, human immunodeficiency virus; CCTA, coronary computed tomography angiography; RCA, right coronary artery; HU, Hounsfield units.

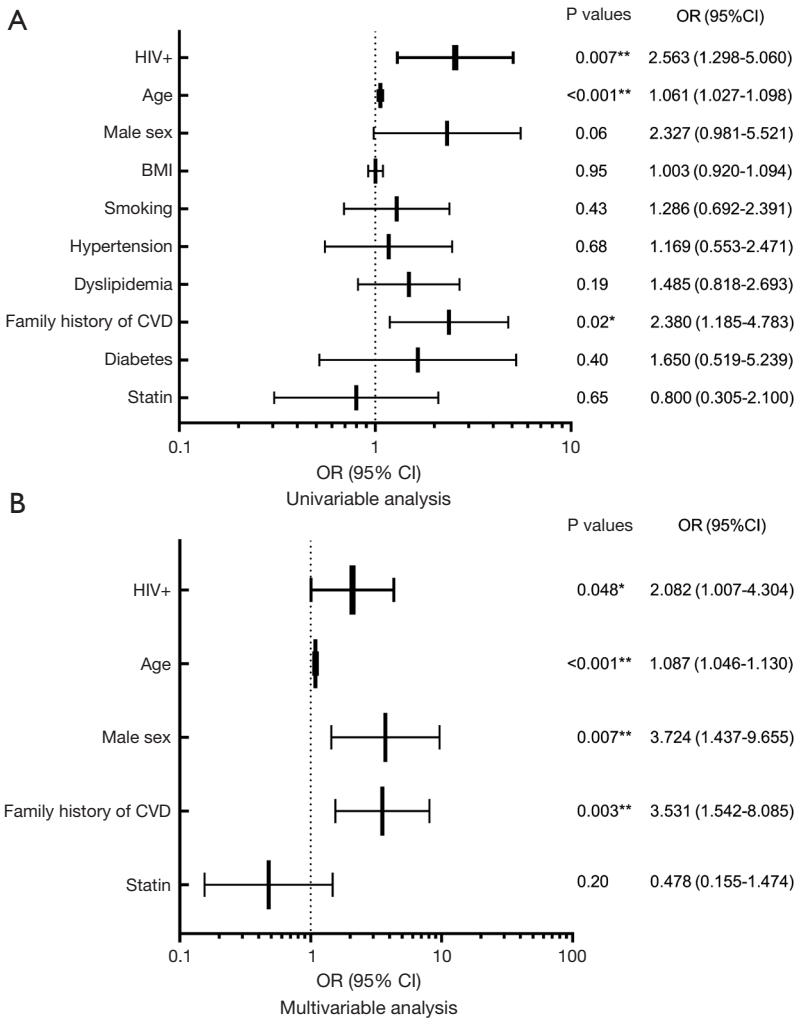

Figure 4 Association between clinical characteristics and noncalcified plaque prevalence. (A) Univariable analysis; (B) multivariable analysis. *, P<0.05; **, P<0.01. HIV, human immunodeficiency virus; BMI, body mass index; CVD, cardiovascular disease; OR, odds ratio; CI, confidence interval.

The correlation between cardiovascular events and the duration of ART or immunosuppression caused by HIV infection is still debatable (36,37). We did not identify any association of ART duration with either calcified or noncalcified plaque, similar to the findings by Tarr *et al.* and Lai *et al.* (21,30). A study suggested that the increased prevalence of noncalcified plaque was associated with the decrease in CD4+ T-cell count, supporting the view that systemic inflammation and immune activation caused by HIV infection facilitate the progression of coronary atherosclerosis (38). In our study, the increased prevalence of noncalcified plaque was associated with nadir CD4+ T-cell count, even after adjustment for cardiovascular risk factors, suggesting that the severity of immunodeficiency before the start of ART is associated with the occurrence of noncalcified plaques. Therefore, the nadir CD4+ T-cell count may be a potential risk factor for subclinical coronary atherosclerosis coronary atherosclerosis in PIWH, even if the current CD4+T cell count is within the normal range after ART, it may lead to subclinical coronary atherosclerosis. The results suggest that early and timely ART should be carried out to reduce the incidence of CAD. Our future studies will investigate associations between coronary atherosclerosis with measures of inflammation and immune activation in PIWH.

Table 4 Multivariable analysis of the relationship between HIV-related variables and plaque prevalence

Variables	Total plaque prevalence		Calcified plaque prevalence		Noncalcified plaque prevalence	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
CD4 current						
>700	Reference					
350–700	0.753 (0.334–1.696)	0.49	0.621 (0.256–1.506)	0.19	1.496 (0.633–3.536)	0.36
<350	1.026 (0.310–3.400)	0.97	1.120 (0.320–3.913)	0.86	1.796 (0.518–6.222)	0.36
CD4 nadir						
>350	Reference					
200–350	0.831 (0.336–2.058)	0.69	0.376 (0.131–1.081)	0.07	1.635 (0.615–4.344)	0.10
100–199	1.474 (0.508–4.276)	0.48	1.102 (0.364–3.337)	0.86	1.713 (0.541–5.419)	0.36
<100	2.295 (0.762–6.912)	0.14	1.226 (0.394–3.812)	0.73	4.139 (1.312–13.060)	0.02*
CD4/CD8						
>1.0	Reference					
0.5–1.0	0.621 (0.264–1.461)	0.28	1.129 (0.427–2.989)	0.41	1.114 (0.453–2.738)	0.81
<0.5	1.354 (0.537–3.412)	0.52	0.678 (0.269–1.711)	0.81	2.038 (0.783–5.304)	0.15
Time of HIV diagnosis (years)						
<5	Reference					
5–10	0.977 (0.424–2.252)	0.96	0.823 (0.331–2.047)	0.68	1.251 (0.523–2.992)	0.62
>10	0.919 (0.371–2.276)	0.85	0.910 (0.342–2.420)	0.85	1.197 (0.464–3.088)	0.71
Time of ART use (years)						
<5	Reference					
5–10	0.721 (0.330–1.576)	0.41	0.663 (0.281–1.569)	0.35	0.920 (0.408–2.073)	0.84
>10	1.469 (0.523–4.132)	0.47	0.904 (0.314–2.604)	0.85	1.878 (0.657–5.373)	0.24
ART regimens						
2 NRTI + 1 NNRTI	Reference					
2 NRTI + 1 PI	1.471 (0.436–4.961)	0.53	1.698 (0.450–6.405)	0.44	1.748 (0.520–5.872)	0.37
Others	0.768 (0.319–1.848)	0.56	0.817 (0.307–2.176)	0.69	0.892 (0.365–2.177)	0.80

Age, sex, statin use, and family history of CVD were adjusted in multivariate analyses. *, P<0.05. HIV, human immunodeficiency virus; OR, odds ratio; CI, confidence interval; ART, antiretroviral therapy; NTRI, nucleoside reverse transcriptase inhibitor; NNTRI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor.

Limitations

There are several limitations in this study. First, this was a cross-sectional analysis; the occurrence of cardiovascular events will be further examined through follow-up in the future. Second, the diagnosis time of HIV infection may not be consistent with the actual time. Hence, it may not be possible to accurately estimate the effect of HIV infection duration on coronary atherosclerosis. In addition, perivascular inflammatory changes were identified primarily by perivascular fat in this study. Atherosclerosis and perivascular fat may be associated with inflammatory biomarkers (such as high sensitivity C-reactive protein and pro-inflammatory cytokines) (39). In the future, we will further collect inflammatory biomarkers. Finally, the sample size of the control group was relatively small, but

it can still initially reflect the characteristics of coronary atherosclerosis in Chinese PIWH. This study also has some advantages. This study explored the correlation between clinical indicators and CCTA-related imaging characteristics in Chinese PIWH, including plaque characteristics and perivascular fat characteristics. Our study was carried out in 1 medical center and 1 ethnic group. In addition, all PIWH enrolled in this study had no previous cardiovascular events, and they were all undergoing ART. Thus, the effects of race, population, or study site could not confound the findings of this study. However, that only 1 ethnic group was included may also be a limitation, as it is uncertain whether the findings are generalizable to other cohorts or populations.

Conclusions

In this study, PIWH had a higher risk of developing noncalcified plaque and greater perivascular fat, suggesting an increased risk for cardiovascular events. The increased prevalence of noncalcified plaque was associated with nadir CD4+ T-cell count. A combination of CCTA and post-processing technology can better stratify the risk of cardiovascular events and monitor progress of CAD in PIWH.

Acknowledgments

Funding: This study was supported by the National Natural Science Foundation of China (No. 82171918); and the Projects of Key Laboratory of AIDS Immunology, Chinese Academy of Medical Sciences (No. 2019PT320019).

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://qims.amegroups.com/article/view/10.21037/qims-24-79/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-24-79/coif). T.L. serves as an unpaid editorial board member of *Quantitative Imaging in Medicine and Surgery*. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Board of The First Hospital of China Medical University (No. 2019-228-2) and informed consent was provided by all participants.

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Cite this article as: Zhou J, Jin S, Ding H, Liu H, Huo H, Peng X, Hou Y, Geng W, Shang H, Liu T. Quantification of subclinical plaque characteristics and perivascular fat using coronary computed tomography angiography (CCTA) among individuals with human immunodeficiency virus (HIV). Quant Imaging Med Surg 2024;14(7):4675-4687. doi: 10.21037/qims-24-79

