Coronary atherosclerosis characteristics in HIV-infected patients on long-term antiretroviral therapy: insights from coronary computed tomography–angiography

Thomas Senoner[a], Fabian Barbieri[a], Agne Adukauskaite[a], Mario Sarcletti[b], Fabian Plank[a], Christoph Beyer[c], Wolfgang Dichtl[a] and Gudrun M. Feuchtner[c]

Objective: The aim of the study was to assess coronary artery disease (CAD) characteristics by coronary computed tomography–angiography (CCTA) in individuals with HIV infection on long-term antiretroviral therapy (ART)

Design: Retrospective case-controlled matched cohort study.

Methods: Sixty-nine HIV-positive patients who underwent 128-slice dual source CCTA (mean age 54.9 years, 26.1% women) with mean 17.8 ± 9.4 years of HIV infection and a mean duration on ART of 13 ± 7.3 years were propensity score-matched (1 : 1) for age, sex, BMI, and five cardiovascular risk factors with 69 controls. CCTA was evaluated for stenosis severity [according to Coronary Artery Disease – Reporting and Data System (CAD-RADS)], total plaque burden [segment involvement score (SIS) and mixed-noncalcified plaque burden (G-score)]. As inflammatory biomarkers, high-risk plaque (HRP) features (napkin-ring sign, low-attenuation plaque, spotty calcification, positive remodeling), perivascular fat attenuation index (FAI), and ectatic coronary arteries were assessed.

Results: CAD-RADS was higher in HIV-positive participants as compared with controls (2.21 ± 1.4 vs. 1.69 ± 1.5, $P = 0.031$). A higher prevalence of CAD and G-score ($P = 0.043$ and $P = 0.003$) was found. HRP prevalence [23 (34.3%) vs. 8 (12.1%); $P = 0.002$] and the number of HRP (36 vs. 10, $P < 0.001$) were higher in HIV-positive individuals. A perivascular FAI greater than −70 Hounsfield units was present in 27.8% of HRP. Ectatic coronary arteries were found in 10 (14.5%) HIV-positive persons vs. 0% in controls ($P = 0.003$).

Conclusion: Noncalcified and HRP burden in HIV-infected individuals on long-term ART is higher and associated with higher cardiovascular risk. Moreover, HIV-positive individuals displayed a higher stenosis severity (CAD-RADS) and more ectatic coronary arteries compared with the control group.

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[a]Department of Internal Medicine III, Cardiology, [b]Department of Dermatology, and [c]Department of Radiology, Innsbruck Medical University, Innsbruck, Austria.

Correspondence to Dr Thomas Senoner, Department of Internal Medicine III-Cardiology, Innsbruck Medical University, Anichstr. 35, A-6020 Innsbruck, Austria.

Tel: +43 512 504 83648; fax: +43 512 504 23264; e-mail: Thomas.Senoner@i-med.ac.at
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Introduction

In 2018, roughly 37 million people live with HIV infection worldwide, with the highest prevalence in countries in sub-Saharan Africa. Worldwide, 21.7 million (59%) are receiving antiretroviral treatment (ART) [1], which has translated a life-threatening virus infection to a chronic disease. Patients who have access and adhere to ART have an excellent virological and immunological response and most of them have a life expectancy similar to HIV-negative individuals.

However, coronary artery disease (CAD) poses a particular threat to individuals with HIV infection in terms of both survival and morbidity, with an 1.5–2-fold increased risk of cardiovascular events [2,3]. The underlying pathomechanism of CAD in HIV-positive individuals are complex and not fully understood. Apart from the high prevalence of cardiovascular risk factors in HIV-infected patients, HIV-accelerated inflammation also seems to be a promotor of CAD [4,5]. Furthermore, the long-term effect on coronary artery disease of metabolic changes induced by some antiretrovirals has not been fully elucidated.

Moreover, studies using computed tomography–angiography (CCTA) for assessment of coronary vessel wall changes in HIV-positive individuals are sparse and contradicting [4,6].

CCTA allows for the differentiation of coronary vessel wall changes indicating atherosclerosis or inflammation. Imaging biomarkers of inflammation represent high-risk plaque (HRP) features and the perivascular fat attenuation index (FAI) [7]. High-risk plaques are defined by CCTA by applying the four major criteria: low-attenuation (lipid-rich) plaque, napkin-ring sing, spotty calcification and positive remodeling. Furthermore, focal ectatic coronary arteries are a sign of increased systemic inflammation [8].

Moreover, CCTA permits quantification of coronary stenosis severity and total plaque burden [9,10], and the differentiation of noncalcified fibroatheroma from calcified plaque.

Thus, the aim of our study was to assess the coronary artery disease profile and signs of plaque inflammation (defined by HRP markers, perivascular FAI, and coronary ectasia) in patients with long-term HIV infection on ART in a retrospective case-controlled matched cohort study.

Methods

Study design

We included patients with low-to-intermediate pretest probability referred to CCTA in the university hospital Innsbruck, Austria, for the evaluation of CAD between June 2007 and June 2018, approved by our local institutional review board (IRB), into our retrospective matched case-controlled cohort study.

The pretest probability was calculated using the updated Diamond and Forrester model [11]. Furthermore, the studied patients had a low-to-intermediate 10-year atherosclerotic cardiovascular disease (ASCVD) risk [12].

Our prospective database included 2888 patients, 72 of whom were HIV-positive. All HIV-positive individuals were 1 : 1 propensity score matched for age, sex, BMI and the following five major risk factors (arterial hypertension, smoking, positive family history, dyslipidemia and diabetes) to controls without a clinical history of HIV infection, defined by a questionnaire prior to CT and a standardized medical checkup exam including blood samples. This yielded 69 patients in each group. Patients in the control group were referred for a CT scan because of the suspicion of an underlying CAD based on patients' symptoms (atypical or stable chest pain, pathological cardiac exercise stress test).

Inclusion criteria for the HIV+ group were:

1. HIV infection tested according to nationwide standards in reference laboratory.
2. Information about: $CD4^+$ T-lymphocyte count (actual numbers and NADIR), duration of HIV-infection, duration of antiretroviral treatment ART (recorded from medical chart).
3. Conventional coronary risk factors according to standardized ESC criteria Arterial hypertension (SBP >140 mmHg or DBP >90 mmHg), dyslipidemia (total cholesterol >200 mg/dl and HDL <40 mg/dl and/or LDL >160 mg/dl), positive family history [myocardial infarction (MI) or sudden cardiac death in an immediate male relative <55 years or female relative <65 years), smoking (current or quit within the last 6 months) and diabetes [13,14].

Exclusion criteria were:

1. Previous percutaneous coronary intervention (PCI).
2. Severe aortic stenosis or other high-grade valvular disease more than 2.
3. Renal dysfunction (serum GFR <45 ml/min per 1.73 m^2), pregnancy, age less than 21 years.
4. Only a coronary calcium score (CCS).

Computed tomography–angiography

A noncontrast ECG-gated CCS with standardized scan parameters (detector collimation 64 mm × 1.5 mm; 120 kV) was done and the Agatston Score calculated. Then, CCTA was appended using either a 64-slice CCTA

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(Sensation 64, Siemens; until December 2009) or 128-slice dual source CCTA thereafter (Definition FLASH, Siemens Healthineers, Erlangen, Germany) with a detector collimation of 2 mm × 64 mm × 0.6 mm, a z-flying spot of 64 mm × 0.6 mm and a rotation time of 0.28 or 0.33 s, respectively. In patients examined with 64-slice CT, retrospective ECG-gating was applied. In patients undergoing 128-dual-source CT, prospective ECG-triggering was used in regular heart rates less than 65 bpm (diastolic padding, 70% of RR-interval) and greater than 65 bpm (systolic padding, 40% RR-interval) whereas retrospective ECG-gating was utilized in irregular heart rates [15]. Iterative reconstructions were used and adjusted if necessary to provide optimal image quality [16]. Beta-blockers were given to all patients who underwent 64-slice CT to lower heart rate under 65 bpm, and to those who underwent 128 dual-source CT only if heart rate (HR) was greater than 80 bpm. Five milliliters metoprolol intravenously was injected prior to CCTA and repeated if deemed necessary after blood pressure control. No patient received sublingual glyceryl trinitrate.

An iodine contrast agent (Iopromide, Ultravist 370) was injected intravenously (flow rate 4–6 ml/s +40 cm^3 saline chaser), triggered into arterial phase [bolus tracking; 100 Hounsfield units (HU) threshold; ascending aorta]. The contrast volume varied between 65 and 120 cm^3 according to the individual patient characteristics. Axial images were reconstructed with 0.75 mm slice width (increment 0.4/medium-smooth kernel B26f I3) during best diastolic and systolic phase.

The mean radiation dose in our institution is 6–7 mSv, according to our monthly dose monitoring. Our institution participated in the PROTECTION VI multicenter trial, which revealed similar results [17].

Computed tomography–angiography image analysis

Curved multiplanar reformations (cMPR) and oblique interactive MPR of all vessels using 3-D postprocessing software (SyngoVia, Siemens) were generated:

1. Coronary stenosis severity was estimated visually as: minimal less than 25%, mild 25–49%; intermediate 50–69% or severe at least 70% according to CAD-RADS [18] per-coronary segment [American Heart Association (AHA)-modified-16-segment classification] [19].
2. Plaque types were defined as: calcified (T1), mixed (dominantly calcified >noncalcified) (T2), mixed (dominantly noncalcified >calcified) (T3), and noncalcified (T4) per coronary segment. Calcified plaque was defined as hyperattenuating with more than 150 HU, noncalcified plaque was defined as hypoattenuating lesions with 150 HU or less [20]. The coronary segment involvement score (SIS) [21] and the G-score (i.e. the sum of plaque types T1–4 for each segment) [22] as marker for an increasing mixed noncalcified/calcified plaque burden were calculated per-coronary segment (AHA-modified-16-segment classification) [19].
3. Subjective HRP analysis [23–25]
   a. Low attenuation plaque (LAP), hypodense relative to the contrasted artery lumen, was screened by utilizing the 'pixel-lens' for the lowest CT-density (HU) area, and then a regions of interest (ROI) was drawn as large as possible, while sparing areas affected by motion, beam hardening or partial volume artifacts. The HU_ROI was measured on three consecutive images (1 mm slice thickness). LAP was defined as 'noncalcified' if more than 150 HU [20].
   b. Napkin Ring Sign (NRS) was defined [23] as LAP with a hyperdense rim and hypodense LAP core.
   c. Spotty calcification was defined as calcification less than 3 mm size within a hypodense plaque.
   d. The remodeling index was calculated as the ratio of the maximal cross-sectional vessel diameter including the plaque and the lumen, and its closest proximal (or distal: in ostial lesions) normal reference vessel lumen diameter.

   A HRP was identified if a minimum of two out of four criteria were present (according to label 'V' – CADRADS) [18]. In case of multiple lesions, all HRPs were quantified and the number of HRP per patient recorded. For LAP, a threshold of 60 HU was set as HRP criterion [25].
1. The perivascular FAI was measured within two ROI adjacent to noncalcified and high-risk lesions, and HU were recorded. A FAI of more than −70 HU and a gradient of more than 10 HU between two ROI were regarded as positive.
2. Ectatic coronary artery segments were defined as vessel diameter increase of more than 50% relative to the adjacent normal sized coronary lumen.

CCTA image analysis were performed by one master observer (>10 years of experience, level III SCCT) and a second independent observer with >6 months of training. Consensus reading was obtained. Plaques with image quality limitations, such as artifacts (motion blurring, high image noise, beam hardening or streak artifacts) were excluded from quantitative HRP analysis. No CCTAs with inadequate image quality were included.

Statistical analysis

Quantitative variables are expressed as means ± SD; categorical variables as absolute values and percentages.

For minimization of possible selection bias and potential confounding, a propensity score matchmaking model was calculated. A binary regression was conducted including age, sex, BMI and the following five major risk factors (arterial hypertension, smoking, positive family history, dyslipidemia, diabetes). Given probabilities were then

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matched by using a 1 : 1 nearest neighbor matchmaking process without replacement. Matching tolerance was set to 0.01, which resulted in 69 pairs.

Differences in all parametric data between two groups were tested using the independent *t*-test in case of normal distribution or Mann–Whitney *U* for nonnormally distributed and rank-scaled variables [such as stenosis severity score (SSS), severity involvement score (SIS), G-score, CCS and CAD-RADS score]. To assess the distribution, the Kolmogorow–Smirnov test and histograms were used. Differences in categorical data were determined with chi-square or Fisher's exact test (if $n < 5$ per group).

Correlations between HRP and duration of ART (<5 years vs. ≥5 years) and HIV infection (<5 years vs. ≥5 years), and $CD4^+$ nadir (<200 cells/μl vs. ≥200 cells/μl), were done using binary logistic regression analysis and adjusted for the five cardiovascular risk factors. Correlations between ART duration and G-score, HIV duration and G-score, and $CD4^+$ cells and G-score were done using linear regression analysis and adjusted for the five cardiovascular risk factors. The nonnormally distributed continuous variables had to be transformed in order to become normally distributed, as previously described [26].

All statistical analyses were done using IBM SSPS software (V25.0; IBM Corporation, Armonk, New York, USA). A *P* value of less than 0.05 was considered significant.

Results

Out of our prospective database (2888 patients between 2007 and 2018, 72 of whom were HIV positive), HIV-positive persons were 1 : 1 propensity score matched with HIV-negative controls, which yielded 69 patients in each group. Two patients in each group only had a CCS without contrast-enhanced CCTA, hence 67 patients in each group were finally included for analysis.

The mean duration of HIV infection was 17.8 ± 9.4 years (minimum 0.19 to maximum 33 years) and patients were on ART for a mean of 13.0 ± 7.3 years (minimum 0 – maximum 24.27 years). The majority of patients were on ART (67 of 69) at the time of CCTA, except for two, in which ART was initiated 1 and 1.3 years after CCTA, respectively.

There was no difference in age, sex and the major risk factors between HIV-positive individuals compared with HIV-negative matched controls (Table 1).

CAD prevalence (any plaque) and more than 50% stenosis were both more prevalent in the HIV-positive cohort compared with the control group ($P = 0.043$ and $P = 0.001$, respectively). The SSS was significantly higher in HIV-positive compared with HIV-negative individuals ($P = 0.038$). Mixed noncalcified plaque burden (G-score) as well as CCS were significantly higher in the HIV-positive cohort compared with the control group ($P = 0.003$; $P = 0.015$, respectively). HIV-positives showed significantly more HRP (number of patients with at least one HRP) compared with the control group (23 vs. 8, $P = 0.003$) and the total number of HRP was higher (31 vs. 10; $P < 0.001$). There was a trend towards higher total plaque burden (SIS) in HIV-infected individuals, although this did not reach statistical significance ($P = 0.06$; Table 2).

A total of 27.8% of HIV-positive individuals displayed a positive perivascular FAI (more than −70 HU). Ectatic coronary arteries were found in 10 (14.5%) individuals with HIV-infection vs. 0% in controls ($P = 0.003$).

Figure 1 shows a patient with long-standing HIV infection (31 years) and who was started on ART about

Table 1. Characteristics of the study cohort at time of cardiac imaging ($n = 138$).

Characteristics	HIV + ($n = 69$)	HIV− ($n = 69$)	*P* value
Mean age (years)	54.9 ± 8.7	52.2 ± 11.4	0.140
Male sex, *n* (%)	51 (73.9)	47 (68.1)	0.574
BMI (kg/m^2),	24.0 ± 4.4	25.8 ± 4.4	0.131
Hypertension, *n* (%)	24 (34.8)	27 (39.1)	0.724
Current smoking, *n* (%)	56 (81.2)	55 (79.7)	1.000
Positive family history, *n* (%)	24 (34.8)	25 (36.2)	1.000
Dyslipidemia, *n* (%)	27 (39.1)	27 (39.1)	1.000
Diabetes, *n* (%)	7 (10.1)	6 (8.7)	1.000
HIV infection (years)	17.8 ± 9.4		
$CD4^+$ current (cells/μl)	668.5 ± 318.9		
$CD4^+$ nadir (cells/μl)	196.3 ± 202.8		
$CD4^+$ nadir less than 50 cells/μl, *n* (%)	17 (24.6)		
On ART, *n* (%)	67 (97.1)		
ART interrupted, *n* (%)	6 (8.7)		
ART duration (years)	13 ± 7.3		

Parametric data are displayed as mean ± SD, and counts as n (%). Positive family history was defined as myocardial infarction or sudden cardiac death in an immediate male relative less than 5 years or female relative less than 65 years. ART, antiretroviral therapy; CCTA, coronary computed tomography–angiography.

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Table 2. Computed tomography–angiography results.

	HIV+ ($n=67$)	HIV− ($n=67$)	*P* value
CAD prevalence (any plaque), *n* (%)	56 (83.6)	46 (68.7)	0.043
SSS, mean ± SD	1.16 ± 1.6	0.95 ± 2.1	0.038
CAD RADS			
0	11	22	
1	11	7	
2	10	21	<0.001
3	23	4	
4	12	13	
Total greater than 50%, *n* (%)	35 (52.2)	17 (25.4)	0.001
CAD RADS, mean ± SD	2.21 ± 1.4	1.69 ± 1.5	0.031
SIS, mean ± SD	3.93 ± 3.0	3.06 ± 3.1	0.067
G-score mean ± SD	10.04 ± 8.5	5.76 ± 5.9	0.003
Calcium score mean ± SD	149.4 ± 287.1	133.2 ± 329.3	0.015
HRP, *n* (%)	23 (34.3)	8 (12.1)	0.002
HRP, *n*	36	10	<0.001
Noncalcifying plaque component, *n* (%)	44 (65.7)	34 (51.5)	0.097
Ectatic coronary segments, *n* (%)	10 (14.5)	0 (0)	0.003

CAD RADS, coronary artery disease reporting and data system; CCS, coronary calcium score; HRP, high-risk plaque; SIS, segment involvement score; SSS, stenosis severity score.

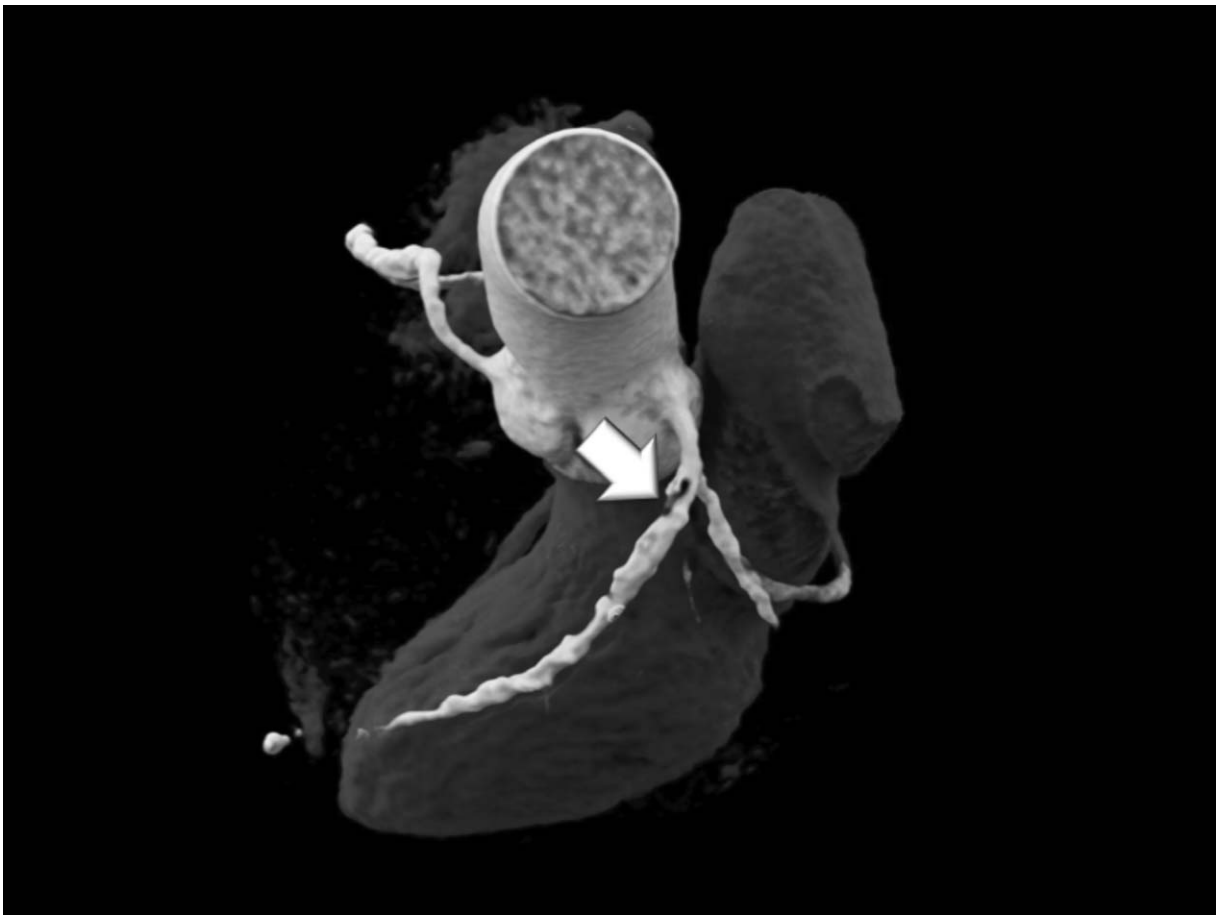

Fig. 1. Sixty-year-old man with four risk factors [arterial hypertension, smoking, positive family history, dyslipidemia (cholesterol 204, low-density lipoprotein 125 mg/dl) and chest pain]. CTA showed a more than 70% stenosis and high-plaque load (G-score 20, SIS score 12), and proximal low attenuation fibrofatty plaque (52 HU). Thirty-one years of HIV infection and 21.5 years on ART. CTA showed and ectatic RCA with a more than 50% stenosis (left panel) and an ectatic LAD with a more than 70% stenosis in the proximal LAD (right panel, white arrow). High-risk plaque in the proximal LAD with low-attenuation fibrofatty plaque (52 HU) (white arrow). CTA, computed tomography–angiography.

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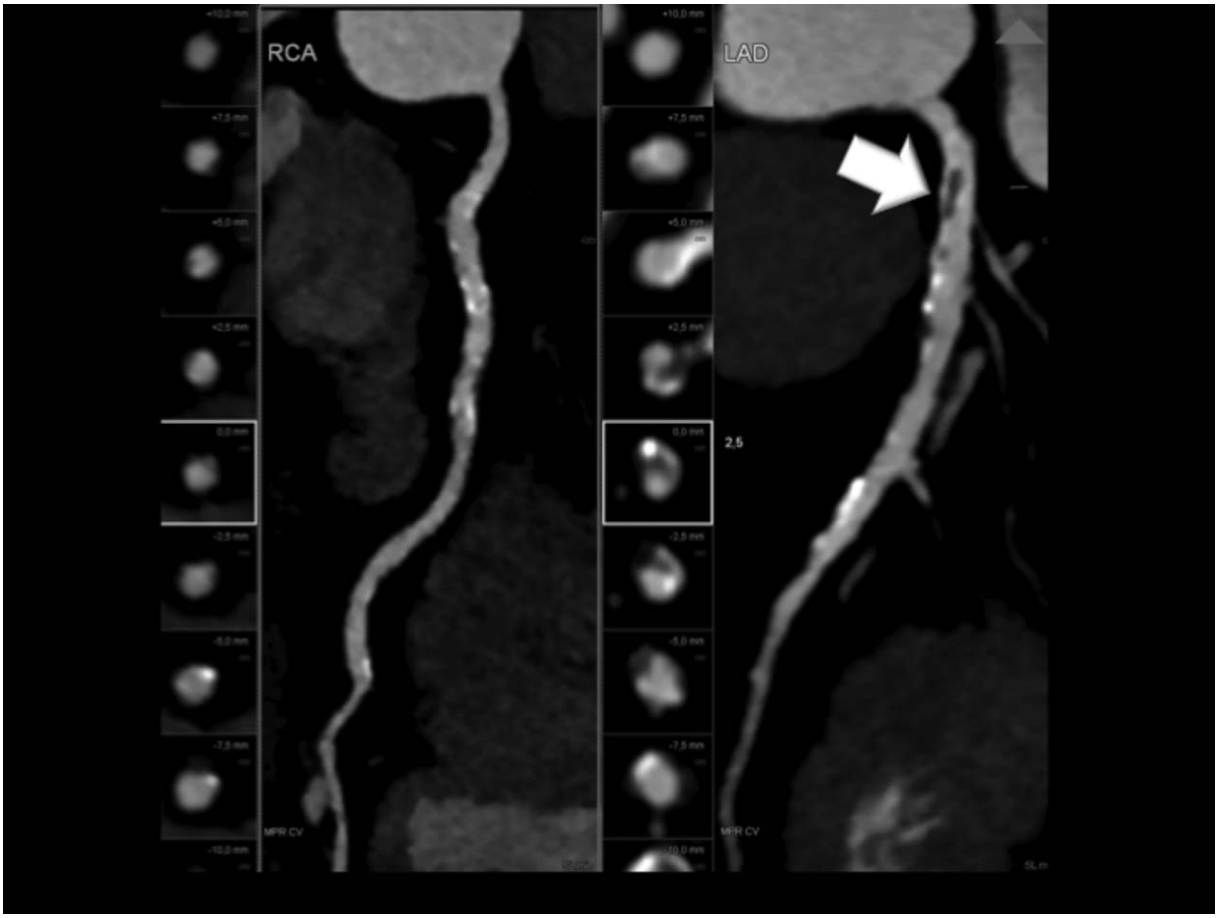

Fig. 1. (Continued).

10 years after diagnosis. This patient has a high plaque burden, more than 70% stenosis in the LAD, as well as a HRP (low-attenuation fibrofatty plaque (52 HU)). Furthermore, the patient's coronary arteries were massively ectatic.

There was no correlation between ART duration and G-score (β, $0.87 \pm$ SE 0.138, $P = 0.529$) (Figure 2a, supplements, http://links.lww.com/QAD/B497), HIV infection and G-score (β, $0.152 \pm$ SE 0.107, $P = 0.159$; Figure 2b, supplements, http://links.lww.com/QAD/B497), and $CD4^+$ cell count and G-score (β, $-0.001 \pm$ SE 0.003, $P = 0.863$; Figure 2c, supplements, http://links.lww.com/QAD/B497), even after adjusting for the five cardiovascular risk factors. Similarly, there was no correlation of the SIS and CCS with HIV infection, ART and $CD4^+$ cell count.

High-risk plaque prevalence did not differ significantly between patients with $CD4^+$ nadir less than 200 and at least 200. High-risk plaque prevalence also did not differ between patients with long-standing HIV infection or ART ($\geq$5 years) compared with individuals with HIV infection or ART less than 5 years (Table 3, supplements, http://links.lww.com/QAD/B497).

About 60% of HIV-infected patients were on statin therapy prior to CCTA examination. Data about the control group regarding the exact number of patients on statin therapy is insufficient, but with about 40% of patients having hypercholesterolemia, we can assume that about 40% were on statin therapy at the time of CCTA.

Discussion

In our study, HIV-positive individuals have higher CAD prevalence, stenosis severity and noncalcified (fibro-fatty) mixed plaque burden. Additionally, an increased number of HRPs was found. High-risk plaque on CCTA have shown a correlation with indirect signs of plaque inflammation, such as thin-cap fibroatheroma with macrophage infiltration by optical coherence tomography [27].

Furthermore, HIV-positive participants showed more indirect signs of perivascular inflammation, such as ectatic coronary segments. Coronary ectasia is an established imaging feature of vasculitis and indicates a chronic inflammatory process. Moreover, we found a high

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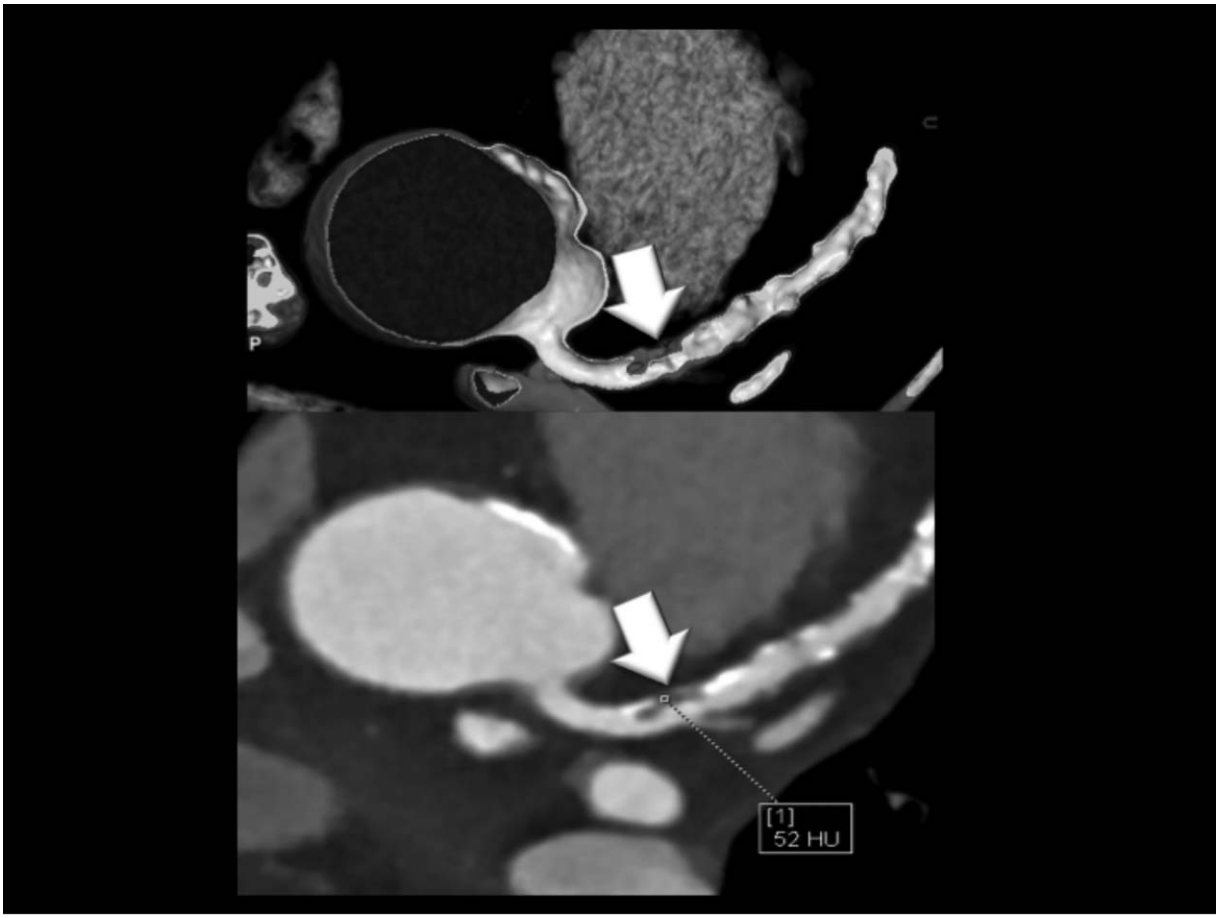

Fig. 1. (Continued).

prevalence of a positive perivascular FAI and a declining perivascular fat attenuation, suggesting perivascular edema and inflammation, which was present in one-third of high-risk lesions.

One landmark multicentric trial (CRISP-CT) has recently shown that the perivascular FAI captures inflammation-induced changes in perivascular fat attenuation and also identifies vulnerable plaques, and thus represents a noninvasive biomarker of coronary inflammation measured by traditional CCTA. An FAI greater than −70 HU resulted in a 5–9-fold increased risk of cardiac death in a cohort of 1872 patients [7,28].

The CCS, another predictor of cardiovascular mortality [29], was also measured in our study. In contrast to our study, mean calcium scores were not higher in HIV+ patients in a meta-analysis including 9000 patients [30]. Reasons might be the longer duration of HIV infection (17.3 vs. 9.3 years) and the longer duration on ART (13 vs. 2.3 years) reported in our study, along with good adherence to ART. Hence, a longer exposure to HIV infection might translate into a higher state of inflammation leading to an increase in coronary calcium [31,32]. Additionally, the higher prevalence of statin medication in the HIV cohort might as well influence the higher calcium score in our cohort. The PARADIGM study has shown that statins reduce especially fibro-fatty and necrotic plaque burden by CCTA, while calcified plaque burden increases [33].

However, the limitation of a calcium score alone is the lack of information regarding noncalcified plaques, which may be even more relevant for risk assessment [34], but can only be detected by CCTA.

Studies have shown a higher prevalence of subclinical coronary atherosclerosis and a greater burden of coronary atherosclerotic plaque, particularly noncalcified inflammatory plaques, in HIV-positive men compared with HIV-negative individuals with similar cardiovascular risk factors. Imaging studies using CCTA have shown a higher prevalence of coronary atherosclerosis in HIV-positive men compared with HIV-negative controls (59.0 vs. 34.4%). Similarly, HIV-positive women had a significantly higher prevalence of noncalcified plaques (74 vs. 23%) compared with HIV-negative female controls [35]. There is a strong association between the presence of HRPs and increased immune activation, with plaques that are prone to rupture being composed of

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a necrotic core with an overlying thin fibrous cap. Vulnerable plaque features (low attenuation, positive remodeling and spotty calcification) are more prevalent in HIV-positive individuals compared with HIV-negative controls [35].

Furthermore, noncalcified coronary artery plaques have been associated with a reduced $CD4^+$ cell count in HIV-positive patients, supporting the notion of systemic inflammatory dysregulation in HIV-positive individuals contributing to CVD. Consequently, systemic inflammation and immune activation in HIV infection contributes to the accelerated atherogenesis seen in HIV-positive individuals [35].

Data using CCTA for assessment of coronary vessel wall changes in HIV-positive individuals are limited and contradicting [4–6].

The Swiss cohort study [4] is the largest series in Europe evaluating coronary artery disease in 428 HIV-positive and 276 HIV−negative individuals, and in both groups, a similar percentage of noncalcified/mixed plaques and HRPs was found, whereas HIV-positive participants had less calcified coronary plaques. This differs from results of the Multicenter AIDS Cohort Study (MACS) evaluating 618 HIV-positive and 383 HIV-negative individuals, which noted a higher prevalence of any plaque and especially of noncalcified plaques in HIV-positive compared with HIV-negative US males, mainly homosexuals [5]. Noncalcified plaques have been shown to correlate with worse long-term clinical outcomes compared with calcified plaques, independent of cardiovascular risk factors and number of diseased coronary arteries [36].

A previous small sample size study on 41 individuals alluded to the inflammatory theory of atherosclerosis by using ^{18}F-FDG-PET and CCTA [6]; however, this has not yet been confirmed in a larger cohort.

Our study results differ from the results of the Swiss HIV cohort study [4]. In our study, HIV-positive participants displayed more HRP, a higher SSS and CCS compared with HIV-negative individuals. In accordance with the Swiss HIV cohort study [4], we found no correlation between ART duration and G-score, duration of HIV infection and G-score, or $CD4^+$ cells and G-score, although a trend could be observed between the duration of HIV infection and higher G-score. The G-score is a measure of a dominant mixed noncalcified plaque burden, weighting fibrofatty atheroma against calcified plaques.

Importantly, total and especially noncalcified plaque burden has been linked with both adverse outcomes (MACE events) [37] and ischemia [38,39]. Even in the absence of severe obstructive CAD (stenosis >70%), a high fibroatheroma and lipid-rich plaque burden is associated with ischemia [40] [INOCA (ischemia and no obstructive coronary artery disease)]. INOCA also explains atypical chest pain complaints and similarly to high-risk plaque, those patients benefit from more intense medical therapy, such as high intense statins or PCSK 9 inhibitors [41,42].

Strengths of our study include the well matched cohorts, which did not differ regarding risk factors as well as age and sex. Furthermore, HIV-positive individuals had a long history of HIV infection (mean 17.8 ± 9.4 years) and were on ART for a mean of 13 ± 7.3 years. Furthermore, only three patients out of 138 (2.17%) were investigated with a 64-slice CT scanner and the rest were all examined with a 128-slice dual source CT scanner (Flash Somatom Siemens). Therefore, the scanner type can be excluded as a source that could potentially influence the results.

Finally, there was no difference in HRP prevalence in those with shorter and longer HIV infection and ART, suggesting that HRPs develop at any stage of HIV infection, though the number of individuals with short-term ART and HIV was low.

Study limitations: We acknowledge the adherent bias related to the retrospective study design. Influencing factors such as the coronary risk profile were minimized by propensity score matching. Only information about statin therapy but not any other medication was included. Furthermore, the inclusion period between HIV-positive individuals and controls differed, with HIV-positive individuals undergoing a CT scan about 1 year prior to controls.

Conclusion

HIV-positive individuals on long-term ART display higher CAD burden and more high-risk plaques.

Furthermore, HIV-infected individuals displayed a higher stenosis severity (CAD-RADS) and more ectatic coronary arteries compared with the control group. Whether targeted therapy reduces cardiovascular events in this at-risk population remains to be evaluated.

Acknowledgements

T.S. and G.M.F. designed the trial. T.S. and F.B. did the statistical analysis. All authors interpreted data. T.S. and G.M.F. drafted the report. All authors provided input into the report and approved the final version of the report.

Conflicts of interest

There are no conflicts of interest.

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