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LaBounty, TM
Hardy, WD
Fan, Z
et al.

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Carotid artery thickness is associated with chronic use of highly active antiretroviral therapy in patients infected with human immunodeficiency virus: A 3.0 Tesla magnetic resonance imaging study

TM LaBounty[1], **WD Hardy**[2], **Z Fan**[3], **R Yumul**[4], **D Li**[3], **R Dharmakumar**[3,5], and **A Hernandez Conte**[4]

[1]Departments of Medicine and Radiology, University of Michigan Medical Center, Ann Arbor, MI, USA

[2]David Geffen School of Medicine, University of California-Los Angeles, Los Angeles, CA, USA

[3]Biomedical Imaging Research Institute, Cedars-Sinai Medical Center, Los Angeles, CA, USA

[4]Department of Anesthesiology, Cedars-Sinai Medical Center, Los Angeles, CA, USA

[5]Heart Institute, Cedars-Sinai Medical Center, Los Angeles, CA, USA

Abstract

Objectives—While patients with HIV infection have an elevated stroke risk, ultrasound studies of carotid artery wall thickness have reported variable results. We hypothesized that subjects with HIV infection on chronic highly active antiretroviral therapy (HAART) would have increased carotid artery wall thickness by magnetic resonance imaging (MRI).

Methods—This cross-sectional study compared carotid artery wall thickness between 26 individuals infected with HIV on chronic HAART and 20 controls, without HIV infection but with similar cardiovascular risk factors, using 3.0-T noncontrast MRI. Inclusion criteria included male gender, age 35–55 years, and chronic HAART (≥3 years) among HIV-seropositive subjects; those with known cardiovascular disease or diabetes were excluded.

Results—Between subjects with HIV infection and controls, there were no differences in mean (± SD) age (47.8 ± 5.0 *vs*. 47.8 ± 4.7 years, respectively; $P = 0.19$) or cardiovascular risk factors ($P > 0.05$ for each). Mean (± SD) wall thickness was increased in those with HIV infection *vs*. controls for the left (0.88 ± 0.08 *vs*. 0.83 ± 0.08 mm, respectively; $P = 0.03$) and right (0.90 ± 0.10 *vs*. 0.85 ± 0.07 mm, respectively; $P = 0.046$) common carotid arteries. Among individuals with HIV infection, variables associated with increased mean carotid artery wall thickness included lipoaccumulation [+0.09 mm; 95% confidence interval (CI) 0.03–0.14 mm; $P = 0.003$], Framingham risk score ≥5% (+0.07 mm; 95% CI 0.01–0.12; $P = 0.02$ mm), and increased duration of protease inhibitor therapy (+0.03 mm per 5 years; 95% CI 0.01–0.06 mm; $P = 0.02$).

Correspondence: Dr Troy LaBounty, University of Michigan Medical Center, 1500 E Medical Center Dr., SPC 5853, Room 2365, Ann Arbor, MI 48109-5853, USA. Tel: 734 764 7440; fax: 734 232 4132; labt@med.umich.edu.

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Conclusions—Individuals with HIV infection on chronic HAART had increased carotid artery wall thickness as compared to similar controls. In subjects with HIV infection, the presence of lipoaccumulation and longer duration of protease inhibitor therapy were associated with greater wall thickness.

Keywords

carotid artery disease; highly active antiretroviral therapy; HIV; magnetic resonance imaging; stroke

Introduction

HIV infection is a leading cause of morbidity and mortality, with over 1 million persons infected and 55 000 new cases annually in the USA alone [1]. Since the introduction of highly active antiretroviral therapy (HAART), HIV infection has become a chronic, treatable disease similar to hypertension and hyperlipidaemia, and life expectancy may approach that of uninfected persons in patients with durably suppressed virus [2–5]. As the population with HIV infection ages, an excess of strokes [6–8] and myocardial infarctions [9,10] has been observed. Comparisons of the carotid artery utilizing ultrasound between individuals with and without HIV infection have provided disparate results, with some studies finding an increase in carotid artery intimal medial thickness among HIV-infected patients as compared with controls [11–15], and other studies observing no difference [16,17]. Existing studies have generally included untreated HIV-infected individuals, and it is not clear whether individuals with HIV infection on chronic, contemporary HAART have increased carotid wall thickness.

We hypothesized that individuals with HIV infection on chronic HAART would have increased carotid artery wall thickness. As carotid artery imaging by magnetic resonance imaging (MRI) may provide results similar to those of ultrasound with reduced inter-procedure variability [18], we utilized 3.0-T MRI to compare carotid artery wall thickness between individuals with HIV infection on ≥3 years of HAART and similar controls. We further evaluated the relationship between selected clinical variables and carotid artery wall thickness among subjects with HIV infection.

Methods

The study recruited 26 HIV-infected subjects on HAART from a single academic medical centre and 20 HIV-negative controls. Inclusion criteria were: male gender, age of 35–55 years, and (for cases only) continuous HAART for ≥3 years. HAART was defined as the use of at least three different anti-HIV medications to achieve viral suppression. Exclusion criteria included history of cardiovascular disease (coronary artery disease, myocardial infarction, stroke or prior revascularization), hepatitis C virus infection, diabetes, prior injecting drug use, prolonged interruptions of HAART (≥3 months), prior AIDS-defining illness and contraindications to MRI. HIV-negative controls were recruited from the same community as the subjects. Control subjects were recruited via subjects’ referral of friends and acquaintances in similar social circles, to approximate the characteristics of those with HIV infection based upon age, race, sexual orientation, lifestyle factors, drug use and medical history, as done previously [19]. This study was reviewed and approved by our Institutional Review Board and all subjects provided written informed consent.

Subjects with HIV infection had high medication compliance (mean 99%; range 90–100%) and 100% had undetectable HIV RNA by polymerase chain reaction (PCR) testing. The mean (±SD) CD4 T-cell count was 682 ± 468 cells/μL (range 242 to 2597 cells/μL). The mean (±SD) duration of HIV diagnosis was 16.8 ±8.1 years (range 4–30 years), and the mean (±SD) duration of HAART was 13.4 ±7.3 years (range 3–28 years). Protease inhibitors had been used in 24 of 26 patients during their treatment history; current protease inhibitors were used in 18 of 24 patients, with all 18 patients utilizing ritonavir as a “booster” PI.

An a priori power analysis was performed to determine the required sample size. To decrease the required sample size of the study, we a priori planned to evaluate the left and right carotid arteries in the same analysis to double our sample size, with a plan to adjust for the potential clustering effect. Based on prior estimates of mean (± SD) carotid intimal medial thickening of 0.62 ±0.11 mm and 0.70 ±0.10 between individuals without HIV infection and individuals with HIV infection on HAART [15], a sample size of 25 subjects in each group with two carotid arteries each was determined to provide 85–89% power to detect a difference in mean carotid artery thickness between groups, using a two-tailed analysis and an alpha of 0.05, and after accounting for a clustering effect for the two arteries with a range of intra-cluster correlations from 0.50 to 0.70. During a pause in enrolment because of changes in study personnel, we performed an interim analysis when 46 of the 50 planned subjects were enrolled. At that time, we identified significant differences between groups, and we terminated subject enrolment early. As we observed significant differences for the separate left and right carotid arteries, a combined analysis that considered the left and right as independent arteries but attempted to correct for intra-subject clustering was no longer needed, and we instead performed separate analyses of the left and right carotid arteries. This eliminated the potential error and statistical assumptions required to estimate the clustering effect for a combined analysis.

All subjects and controls completed a detailed medical and social history questionnaire. For patients with HIV infection, medical records were reviewed to provide details regarding HIV medical and treatment history. A physical examination was performed by an experienced infectious disease specialist to assess anthropometric variables, including the presence of lipodystrophy, defined as the pathological presence (lipoaccumulation) or absence (lipoatrophy) of adipose tissue in various anatomical locations consistent with HAART-associated side effects, consistent with reported in previous literature [20]. If lipodystrophy was present, further physical evaluation was performed to determine the presence of lipoaccumulation and/or lipoatrophy. Height, weight, waist circumference and hip circumference were measured for each subject.

Subjects were instructed to abstain from caffeine, alcohol and vigorous exercise for at least 24 h before all MRI procedures. A fasting, venous blood sample was obtained for the measurement of glucose, lipids, a complete blood count and a basic metabolic panel. In control subjects, HIV testing was performed to confirm the absence of HIV infection. All subjects with HIV infection had prior serological testing that confirmed the diagnosis.

Framingham cardiac risk factor scoring was calculated according to standard criteria, accounting for age, cholesterol, smoking history and blood pressure [21].

All MRI was performed using a 3.0-Tesla whole-body scanner (Magnetom Verio; Siemens Healthcare, Erlangen, Germany) and a bilateral four-channel carotid surface coil (Machnet BV; Eelde, The Netherlands). Subjects were scanned in a head-first supine position. This study utilized images without the use of intravenous contrast. Multislice two-dimensional (2D) time-of-flight imaging was first performed to localize the left and right carotid artery bifurcation. The acquired images were also used to create minimal-intensity-projection images that were later used for positioning the vessel wall scan planes perpendicular to the axis of each common carotid artery. Typical scan parameters were as follows: repetition time/echo time = 22/5 ms; flip angle = 52°; slice thickness = 3 mm with an inter-slice gap of 3 mm; 30 slices; matrix size = 256 × 204; field of view 220 × 175 mm^2; in-plane spatial resolution = 0.86 × 0.86 mm^2.

Dedicated T1-weighted dark-blood imaging was performed separately for the left and right common carotid arteries, with imaging obtained over a 36 mm length in 2 mm increments proximal to the bifurcation of each common carotid artery. A multi-slice 2D T_1-weighted turbo spin echo sequence with spatial pre-saturation band-based dark-blood preparation was used. Sequence parameters were: axial imaging orientation; 18 slices; slice thickness = 2 mm; matrix size = 256 × 256; field of view = 160 × 160 mm^2; in-plane spatial resolution = 0.625 × 0.625 mm^2; repetition time/echo time = 800/12 ms; echo train length = 7; and echo train duration = 63 ms. Chemically selective fat suppression was applied to improve the definition of the outer wall boundary and avoid chemical shift artifacts.

As done previously, a short-axis image was selected for each common carotid artery immediately inferior to the carotid bulb and within 2 cm of the bifurcation [22]. Existing literature has demonstrated good agreement between carotid intimal medial thickness and MRI utilizing semi-automated measurements of the carotid wall [18]. Although proprietary automated tools have been developed, these are not commercially available or validated, so we averaged the diameter of the arterial wall from eight evenly distributed sites manually measured on the short-axis image. In addition, the cross-sectional external area and luminal area of each common carotid artery area were manually traced on the same short-axis images, with the difference of these representing the cross-sectional wall area including the vessel wall and any plaque (Fig. 1). The wall area was indexed to the external area (wall area/external area), as described previously [23]. The presence of any visible carotid artery plaque was defined as visible wall thickening on any slice that was observed in at least two consecutive slices. Carotid artery distensibility was calculated in a manner consistent with the literature, using the mean diameter derived from tracing the cross-sectional area of each artery at end-systole and end-diastole [distensibility coefficient = (2 × change in diameter/end-diastolic diameter/pulse pressure] [22] using bright-blood cine images. A single blinded experienced reader performed all carotid measurements, using OSIRIX version 5.8.1 for Mac OS X (OsiriX Foundation, Geneva, Switzerland). To minimize any bias, cases and controls were read in a random sequence, and the reader was blinded to all clinical variables including HIV status.

Our primary endpoint was a comparison in mean carotid artery thickness between groups. Secondary endpoints included comparisons of the cross-sectional wall area, indexed wall area, the presence of visible carotid artery plaque, and carotid artery distensibility. Comparisons of continuous variables were performed using Student's t-test for variables with normal distributions or the Mann–Whitney U-test for variables without a normal distribution. Fisher's exact test was used for comparisons of categorical variables.

We further assessed clinical and laboratory characteristics among those with HIV infection to determine which of these variables might be associated with increased carotid artery wall thickness. These comparisons were performed using linear regression analysis that utilized the mean value of the left and right common carotid arteries for each patient. Statistical analyses were performed using IBM SPSS version 20 (IBM Corporation, Armonk, NY, USA) for Mac OS X.

Results

Patients with HIV infection (n = 26) and controls (n = 20) did not have statistically significant differences with regard to demographics, medical history, body mass index, medication use (excluding antiretrovirals), blood pressure, fasting cholesterol and glucose, and Framing-ham risk score (Table 1). HIV-infected patients were more likely to report previous noninjecting illicit drug use, and had higher rates of clinical lipodystrophy and greater resting heart rates.

HIV-seropositive subjects had increased bilateral common carotid artery wall thickness as compared with controls, while no differences were observed in external Cholesterol and glucose values and Framingham risk scores were missing for one patient with HIV infection and one control. BMI, body mass index; HDL, high-density lipoprotein; IQR, interquartile range; LDL, low-density lipoprotein; MSM, men who have sex with men; SD, standard deviation. vessel area, luminal area, wall area, normalized wall area or carotid distensibility index (Table 2).

The relationship between relevant clinical characteristics and carotid wall thickness in subjects with HIV infection is provided in Table 3. The presence of clinical lipodystrophy (specifically lipoaccumulation), an increased Table 2 Carotid artery findings Framingham risk score, and greater duration of protease inhibitor therapy were each associated with increased carotid wall thickness.

There was a trend for increased time from HIV diagnosis to be associated with greater carotid wall thickness in linear regression (P = 0.08). In comparison to subjects with a shorter time from diagnosis, those with a time from HIV diagnosis of ≥10 years (≥25th percentile) were observed to have a significant increase in mean carotid artery wall thickness [+0.07 mm; 95% confidence interval (CI) 0.01–0.13 mm; P = 0.049], while no significant difference was observed in subjects with a time of ≥17 years (≥50th percentile) from HIV diagnosis (+0.02 mm; 95% CI –0.03–0.08; P = 0.40).

A longer duration of HAART was not associated with a difference in mean carotid artery wall thickness (P = 0.29), and no significant mean differences were observed in subjects with ≥6 years (≥25th percentile) of HAART (+0.10 mm; 95% CI –0.01–0.11; P = 0.10) or ≥14 years (≥50th percentile) of HAART (+0.01 mm; 95% CI –0.05–0.07; P = 0.78) in comparison to those with a shorter duration of HAART.

We further examined HIV-positive subjects stratified by treatment or no treatment with 'high-risk' antiretroviral agents. These 'high-risk' agents were those previously noted to be associated with an increased risk of myocardial infarction, and included: protease inhibitors, including amprenavir, fosamprenavir, indinavir and lopinavir, Table 3 Variables associated with mean carotid artery wall thickness in patients with HIV infection The mean value of the left and right common carotid wall thickness was used for each patient. Cholesterol and glucose values and Framing-ham risk scores were missing for one patient with HIV infection and one control. CI, confidence interval; HAART, highly active antiretroviral therapy; HDL, high-density lipoprotein; LDL, low-density lipoprotein; NRTI, nucleoside reverse transcriptase inhibitor; PI, protease inhibitor. and nucleoside reverse transcriptase inhibitors, including abacavir and didanosine [9,24–26]. Any use of "high-risk" protease inhibitors was observed in 77% (20 of 26) of subjects, and was not associated with a significant difference in carotid artery mean wall thickness (+0.04 mm; 95% CI –0.03–0.10; P = 0.31). Prior use of "high-risk" nucleoside reverse transcriptase inhibitors was noted in 46% (12 of 26) of HIV-seropositive subjects, and was also not associated with a difference in mean wall thickness (+0.03 mm; 95% CI –0.03–0.09; P = 0.27).

Discussion

This study found that HIV-infected individuals receiving HAART for > 3 years had increased carotid artery wall thickness on MRI compared with HIV-negative controls, despite similar cardiovascular risk factors. Furthermore, among these HIV-seropositive subjects, increased wall thickness was associated with lipoaccumulation, elevated Framingham risk score, longer duration of protease inhibitor therapy, and a time from HIV diagnosis of ≥10 years.

Several carotid artery ultrasound studies have reported an increase in carotid intimal medial thickness among subjects with HIV infection compared with controls [11,13–15], while other studies have reported no significant differences between groups [16,17].

These studies examined heterogeneous populations, and generally included both treated and untreated subjects. In comparison, this study examined patients with HIV infection on chronic HAART, as this represents a group of individuals more likely to survive to an older age and to have an increased risk of cardiovascular events. All of our HIV-infected subjects had undetectable viral loads and high rates of medication adherence, suggesting an optimal HAART response. We further examined a relatively young population without known cardiovascular disease but with a significant time from HIV diagnosis (mean 16.8 years) and duration of HAART therapy (mean 13.4 years), which would be expected to have a low rate of carotid atherosclerosis absent HIV infection and concomitant use of HAART. These findings suggest that, despite optimal medical management of HIV infection with contemporary HAART regimens, a relatively young cohort of individuals with HIV infection may remain at increased risk for subclinical carotid artery atherosclerosis.

This study identified a positive relationship between clinical lipodystrophy and carotid wall thickness in patients with HIV infection on chronic HAART, which may be related to metabolic alterations in this population [27]. While these results contrast with those of a prior study using ultrasound [15], these discordant results may be explained by differences in the examined populations, imaging modality and measurement techniques. It is important to note that, in comparison to ultrasound measurement of the intima and media, MRI measurement includes the adventitial layer, which may result in larger measurements. Nevertheless, in comparison to B-mode ultrasound, which only images two opposing points of the wall, MRI permits cross-sectional imaging; this has been demonstrated to correlate highly with ultrasound but with lower variability, potentially reducing the required sample size for clinical studies [18].

Prior studies that included individuals with untreated HIV infection have reported decreased arterial distensibility by carotid artery ultrasound [14,15,28]. In contrast, the present study observed no change in carotid distensibility using MRI. It is possible that changes in distensibility are obviated in patients with well-controlled HIV infection on chronic HAART or with no evidence of systolic hypertension, although future study may be needed to investigate this issue further.

Increased carotid artery wall thickness was associated with prolonged exposure to protease inhibitors, while no significant relationship was observed with the overall duration of HAART. This is consistent with prior studies using carotid ultrasound [29], and reports of increased myocardial infarctions associated with exposure to pro-tease inhibitors but not to other antiretroviral medication classes [26]. It is also possible that increased duration of protease inhibitor use may be related to a longer time from HIV diagnosis; a larger study would be needed to investigate this potential relationship.

Limitations of this study include its small size, and multivariable adjustments and comparisons between treatment regimens could not be adequately performed as a result. In addition, while observed differences in carotid artery wall thickness were statistically significant, the magnitude of these differences was small (as reported in ultrasound studies); additional study in larger populations is needed to confirm these results. Further, this study was limited to men, and future research in women may be warranted. In addition, men with HIV infection often have disproportionate rates of cardiovascular risk factors and substance abuse, and such variables may be incompletely accounted for in analyses comparing these patients with controls. Finally, lipodystrophy was diagnosed on physical examination by infectious disease physicians experienced in assessing the presence of lipodystrophy in patients with HIV infection, but was not quantitatively determined by imaging. Future studies should consider quantitative imaging measurement of lipodystrophy to validate these findings.

In conclusion, individuals with HIV infection receiving chronic HAART had increased carotid artery wall thickness on MRI as compared with a control group similar in terms of age, gender and cardiovascular risk factors. Furthermore, we demonstrated that the presence of lipoaccumulation and longer duration of exposure to pro-tease inhibitors were associated with greater carotid wall thickness. Future studies are needed to determine whether increased carotid artery wall thickness is associated with an increased risk of stroke, and to determine the mechanism contributing to these findings.

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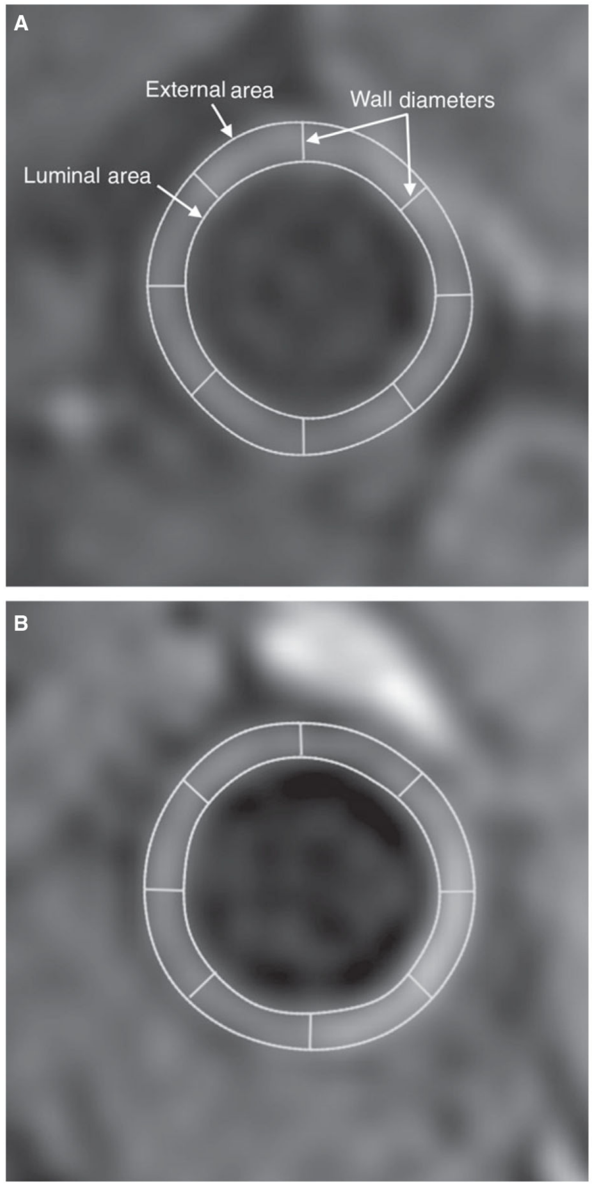

Fig. 1.

Measurement of common carotid artery wall thickness by magnetic resonance angiography. Both patients were 45-year-old men with no cardiovascular risk factors. The left common carotid mean wall thickness was 0.88 mm in the patient with HIV infection on chronic highly active antiretroviral therapy (HAART) (a), and 0.82 mm in the control patient (b). The external carotid area and luminal area are traced for each (labelled), and the wall thickness represents the mean of the eight diameters (two are labelled).

Table 1

Patient characteristics

	HIV-positive (*n* = 26)	HIV-negative (*n* =20)	*P*
Patient demographics			
Caucasian (%)	96	90	0.57
Age (years) (mean ±SD)	47.8 ±5.0	47.8 ± 4.7	0.19
Sex, male (%)	100	100	1.0
Prior MSM (%)	100	100	1.0
Past history			
Hypertension (%)	19	0	0.06
Hyperlipidaemia (%)	38	20	0.21
Tobacco use (any) (%)	23	10	0.44
Illicit drug use (any) (%)	65	20	0.003
Exam findings			
BMI (kg/m^2) (mean ±SD)	25.4 ±3.9	23.9 ± 3.5	0.19
Hip circumference (cm) (mean ±SD)	96.2 ±7.2	95.9 ± 8.2	0.93
Waist circumference (cm) (mean ±SD)	90.8 ±11.8	86.0 ± 13.6	0.22
Waist-to-hip ratio (mean ±SD)	0.94 ±0.09	0.89 ± 0.10	0.10
Lipodystrophy (any) (%)	81	25	<0.001
Lipoaccumulation (%)	69	20	0.001
Lipoatrophy (%)	65	10	<0.001
Medications			
Statin (%)	38	20	0.21
Aspirin (%)	15	10	0.37
Anti-hypertensive (%)	15	0	0.12
Haemodynamics			
Systolic blood pressure (mmHg) (mean ±SD)	115.4 ±15.4	120.4 ± 14.4	0.27
Diastolic blood pressure (mmHg) (mean ±SD)	70.7 ±9.3	67.2 ± 7.1	0.17
Resting heart rate (beats/min) (mean ±SD)	75.5 ±10.9	59.6 ± 9.9	<0.001
Laboratory tests (fasting)			
Glomerular filtration rate (mL/min) (mean ±SD)	83.2 ±21.0	85.1 ± 15.2	0.74
Total cholesterol (mg/dL) (mean ±SD)	172.4 ±32.7	185.0 ± 36.4	0.24
HDL cholesterol (mg/dL) (mean ±SD)	49.6 ±11.8	56.0 ± 14.8	0.12
LDL cholesterol (mg/dL) (mean ±SD)	96.2 ±26.4	93.3 ± 31.3	0.75
Triglycerides (mg/dL) (mean ±SD)	133.0 ±81.3	180.0 ± 97.3	0.09
Glucose (mg/dL) (mean ± SD)	90.3 ±10.3	97.2 ± 14.4	0.07
Glucose ≥ 100 mg/dL (%)	42	7	0.01
Risk profiles			
Framingham risk score [median (IQR)]	3 (2–6)	3 (1– 4)	0.81

Table 2

Carotid artery findings

	HIV-positive (*n* =26)	HIV-negative (*n* = 20)	*P*
Wall thickness diameter (mm)			
Left	0.88 ± 0.08	0.83 ±0.08	0.03
Right	0.90 ± 0.10	0.85 ±0.07	0.046
Eternal area (mm^2)			
Left	53.0 ± 6.8	50.3 ±6.6	0.17
Right	55.3 ± 6.0	51.9 ±9.3	0.14
Luminal area (mm^2)			
Left	32.7 ± 5.5	31.2 ±4.9	0.34
Right	33.8 ± 4.3	32.0 ±6.9	0.27
Wall area (mm^2)			
Left	20.3 ± 2.2	19.1 ±2.2	0.06
Right	21.4 ±3.0	19.9 ±2.9	0.09
Normalized wall area			
Left	0.39 ± 0.03	0.38 ±0.03	0.68
Right	0.39 ± 0.04	0.39 ±0.03	0.86
Diameter change (systole–diastole) (mm)			
Left	0.70 ± 0.23	0.72 ±0.16	0.67
Right	0.70 ± 0.17	0.73 ±0.20	0.60
Carotid distensibility index (10 ±^{3}/kPa)			
Left	36.6 ± 10.1	33.5 ±7.6	0.30
Right	36.6 ± 10.1	32.9 ±9.6	0.21
Any visible carotid artery plaque			
Left	4	0	1.0
Right	0	0	1.0

Values are provided as percentage or mean ±standard deviation.

Table 3

Variables associated with mean carotid artery wall thickness in patients with HIV infection

	Change in wall thickness (mm)		
	Estimate	**95% CI**	**p**
Patient characteristics			
Age (per 10 years)	0.05	−0.01−0.11	0.06
Exercise level ≥2 (*vs.* < 2)	−0.03	−0.09−0.04	0.42
Past history			
Hypertension	0.04	−0.03−0.11	0.27
Hyperlipidaemia	0.01	−0.05−0.07	0.83
Tobacco use	0.01	−0.05−0.07	0.71
Illicit drug use	0.03	−0.03−0.09	0.28
Physical exam findings			
Body mass index (per 5 kg/m^2)	0.02	−0.02−0.06	0.27
Waist-to-hip ratio (per 1)	0.23	−0.08−0.55	0.14
Lipodystrophy (any)	0.07	0.01−0.14	0.047
Lipoaccumulation	0.09	0.03−0.14	0.003
Lipoatrophy	−0.01	−0.06−0.06	0.98
Medications			
Statin	0.01	−0.05−0.07	0.68
Aspirin	−0.04	−0.12−0.04	0.35
Anti-hypertensive	0.04	−0.04−0.12	0.29
Plasma metabolites (fasting)			
Total cholesterol (per 10 mg/dL)	0.01	−0.01−0.02	0.16
HDL cholesterol (per 10 mg/dL)	−0.02	−0.04−0.01	0.18
LDL cholesterol (per 10 mg/dL)	0.01	−0.01−0.02	0.12
Triglycerides (per 10 mg/dL)	0.01	−0.01−0.01	0.20
Glucose ≥100 mg/dL	0.01	−0.10−0.12	0.84
Risk profiles			
Framingham risk score ≥5% (*vs.* < 5%)	0.07	0.01−0.12	0.02
HIV history			
Time from HIV diagnosis (per 5 years)	0.02	−0.01−0.03	0.08
Duration of HAART (per 5 years)	0.01	−0.01−0.03	0.29
Duration of PI therapy (per 5 years)	0.03	0.01−0.06	0.02
Duration of NRTI therapy (per 5 years)	0.01	−0.01−0.02	0.90

The mean value of the left and right common carotid wall thickness was used for each patient. Cholesterol and glucose values and Framing-ham risk scores were missing for one patient with HIV infection and one control.

CI, confidence interval; HAART, highly active antiretroviral therapy; HDL, high-density lipoprotein; LDL, low-density lipoprotein; NRTI, nucleoside reverse transcriptase inhibitor; PI, protease inhibitor.