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Associations of antiretroviral drug use and HIV-specific risk factors with carotid intima–media thickness

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Abstract

Background—Previous research has demonstrated an increase in carotid intima–media thickness (cIMT) in HIV-infected individuals compared to controls. However, the reason for this increased level of subclinical vascular disease is unknown.

Objective—To identify HIV-related risk factors for increased cIMT.

Methods—We evaluated the relationship between HIV-related characteristics (including markers of HIV disease severity and use of antiretroviral therapy) and cIMT measurements in the internal/bulb and common carotid regions among 538 HIV-infected participants from the Study of Fat Redistribution and Metabolic Change in HIV Infection (FRAM). We used Bayesian model

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averaging to estimate the posterior probability of candidate HIV and non-HIV-related risk factors being true predictors of increased cIMT. Variables with a posterior probability of more than 50% were used to develop a selected regression model for each of the anatomic regions.

Results—For common cIMT, the Bayesian model selection process identified age, African-American race, and systolic and diastolic blood pressure with probability more than 95%, HDL cholesterol with probability 85% and Hispanic ethnicity with probability 51%. Among the HIV-related factors included in the analysis, only tenofovir use was selected (51% probability). In the selected model, duration of tenofovir use was associated with lower common cIMT (−0.0094 mm/year of use; 95% confidence interval: −0.0177 to −0.0010). For internal cIMT, no HIV-related risk factors were above the 50% posterior probability threshold.

Conclusion—We observed an inverse association between duration of tenofovir use and common carotid cIMT. Whether this association is causal or due to confounding by indication needs further investigation.

Keywords

atherosclerosis; carotid intima–media thickness; HIV; tenofovir

Introduction

Since the introduction of highly active antiretroviral therapy (HAART) as a treatment for HIV infection, life expectancy has increased markedly among HIV-infected persons [1].

However, this increase in life expectancy appears to be coupled with an increase in cardiovascular events – including myocardial infarction [2]. The reasons for the increase in cardiovascular risk among HIV-infected persons remain controversial, and there is debate over the extent to which it is attributable to HIV-related differences in traditional risk factors, HIV infection itself, or the use of antiretroviral medications [3]. Even after adjustment for traditional risk factors, it is difficult to separate the effects of HIV infection itself from those due to antiretroviral therapy that is used almost universally in industrialized nations.

One approach to detecting and understanding this increased cardiovascular risk among HIV-infected persons is the use of markers of preclinical vascular disease or atherosclerosis. Higher levels of carotid intima–media thickness (cIMT) predict serious adverse cardiovascular events in the general population [4,5]. In the second exam of the Study of Fat Redistribution and Metabolic Change in HIV Infection (FRAM), cIMT was used to demonstrate that HIV-infected participants had an increased level of subclinical vascular disease when compared to controls, even after accounting for traditional cardiovascular risk factors [6]. It is unknown whether the observed higher cIMT is due to HIV infection itself or if it could be a consequence of antiretroviral therapy.

Some previous studies have suggested that there may be an association between the use of protease inhibitors and increased cIMT [7–10]. However, most of these studies were not able to adjust for all traditional risk factors [8–11]. Other work has suggested that any effect due to protease inhibitors may be small compared to traditional risk factors [12–16]. Research has also shown that factors related to HIV disease severity (as opposed to anti-retroviral therapy) may be associated with increased cIMT [17]. More recently, it has been postulated that some of the newer antiretrovirals, which are not associated with a worsening of the metabolic profile, may actually be cardioprotective [18]. Many previous HIV studies have focused on common cIMT [8,12,17–20] due to ease of reproducible reading; a few, however, have considered both internal and common cIMT [6,16]. Recent evidence suggests

that differences between HIV-infected and control participants may be more pronounced in the internal cIMT [6,21].

A primary objective of the second exam of FRAM was to determine whether differences in HIV disease severity or antiretroviral therapy are associated with cIMT in models that tested the contribution of traditional cardiovascular disease (CVD) risk factors. To that end, we used Bayesian model averaging (BMA) [22] to select characteristics associated with cIMT among 538 HIV-infected participants with cIMT measurements.

Methods

Study population

The FRAM study was initially designed to evaluate the prevalence and correlates of changes in fat distribution, insulin resistance, and dyslipidemia in a representative sample of HIV-infected participants in the United States. The second examination of the FRAM study added measurements of cIMT to study preclinical vascular disease in HIV infection. HIV-infected participants were initially recruited from 16 HIVor infectious disease clinics or cohorts. The methods of the FRAM study have been described in detail previously [23]. FRAM enrolled 1183 HIV-infected participants between 2000 and 2002, with a follow-up exam conducted approximately 5 years later that examined 581 HIV-infected participants who had participated in FRAM 1; of whom 538 had at least one carotid ultrasound (and thus were eligible for inclusion in the study). All HIV-infected participants who had cIMT measurements available (n = 538) were included in this analysis. The FRAM study protocol was approved by institutional review boards at all sites.

Data collection

Demographic information, personal and family medical history was assessed by structured questionnaires of FRAM participants. Past and current medication use was determined by chart review and questionnaires. Height, weight, and blood pressure (BP) were measured by standardized protocols. A fasting venous blood sample was collected from participants for measurement of glucose, lipids, high-sensitivity C-reactive protein, interleukin-6, fibrinogen, and HIV-specific factors (such as viral load and CD4 cell count). We classified participants as having diabetes if they had a fasting blood glucose level of at least 126 mg/dl (7.0 mmol/l) or reported use of insulin or oral hypoglycemic medication.

Assessment of carotid intima–media wall thickness

Trained sonographers at each field center performed B-mode ultrasonography of the near and far walls of the common and internal carotid artery on HIV-infected participants. A standardized protocol was developed by the Ultrasound Reading Center (Tufts-New England Medical Center). Ultrasound images were analyzed centrally at the Ultrasound Reading Center to calculate maximum near- and far-wall cIMT at each arterial segment (common, internal, bulb). The maximal wall thickness (over a series of different measurement sites) of the common carotid artery was computed as the mean of the maximum cIMT of the near and far walls of the right and left sides (available measurements ranged from 0.50 to 1.77 mm). Maximal cIMT of the internal carotid artery was computed in the same way except in a different region of the carotid artery and included both the internal, bifurcation, and the bulb region (available measurements ranged from 0.50 to 3.90 mm).

As a sensitivity analysis, we also defined internal and common carotid artery plaque according to criteria in the Atherosclerosis Risk in Communities (ARIC) study [24–26]. Mean CCA IMT was defined as the mean of the mean far wall common carotid IMT,

excluding segments where IMT was more that 50% larger than base IMT [26]. Max ICA IMT was defined as the maximum of the far wall internal cIMT on either the right or left sides, with plaque defined as presence of any max ICA IMT greater than 1.5 mm.

Some participants had multiple readings due to quality control measures in the FRAM study. Those participants with multiple measures were included as separate observations for each measurement and repeated measures were handled using statistical analysis.

Statistical analysis

We used BMA [22,27] to estimate the posterior probability of a variable being a true predictor for cIMT. Separate models were constructed for internal and common cIMT. BMA has been previously used to develop predictive models in observational data [28] and appears to out-compete traditional model selection approaches in predictive power [29]. The current analysis uses the posterior probabilities of the BMA-based model to select covariates for a regression model; Hoeting *et al.* [30] proposed this method as a way to use BMA to give information about inclusion of individual predictors while still utilizing traditional selected models. We, therefore, use BMA to identify predictors of interest and then present traditional models to enhance comparability with other studies of cIMT [7–21].

We retained all predictors that had a posterior probability of at least 50%; posterior probabilities of 50–75% roughly correspond to low levels of statistical significance in classical modeling in small samples [22]. We used linear generalized estimating equations (GEE) (with robust confidence intervals), because of the presence of repeated measures on some participants [6], to model the associations between the risk factors that were identified by BMA and cIMT. Continuous variables were modeled as linear terms in the statistical model (although testing for logarithmic transformations was considered during the model development stage). The small amount of missing data (~2%) present in a subset of predictors was handled using multiple imputation [31]. Bayesian model selection was performed using the BMA package with bicreg command in the R statistical computing language, and linear GEE was performed using PROC GENMOD in SAS version 9.2. An uninformative prior was used for all Bayesian analysis, which makes the BMA approach more conservative than simply selecting the best fitting model. As a secondary analysis, we performed the BMA excluding lipids and diabetes.

As a sensitivity analysis, we also used BMA to estimate the posterior probabilities for candidate predictors of the ARIC-defined common cIMT, internal cIMT, and internal plaque. We then used linear generalized estimating equations to model the associations of the risk factors that were identified by BMA with ARIC-defined cIMT. Any variable with a posterior probability at least 50% for any definition of cIMT was retained in the model. Results of these sensitivity analyses are included in an online supplement.

Results

The characteristics of all participants are presented in Table 1. The FRAM participants cover a broad age range, a number of races/ethnicities and different HIV-specific risk factors.

Table 2 presents the frequency and mean duration of antiretroviral medication use among FRAM participants. Mean duration of treatment among those participants who took a given class of agent was 4.6 years for protease inhibitor, 2.6 years for non-nucleoside reverse transcriptase inhibitors (NNRTIs), and 8.2 years for nucleoside reverse transcriptase inhibitors (NRTIs). Nearly all participants had a history of antiretroviral medication treatment (84% treated with a protease inhibitor, 70% treated with a NNRTI, and 97% treated with a NRTI).

The posterior probabilities of a variable being selected for a statistical model based on a BMA approach are displayed in Table 3. Several traditional risk factors were selected as potential predictors based on a posterior probability of at least 50% (age, race or ethnicity, BP, smoking, and lipid profiles) for at least one cIMT segment (common or internal). The posterior probability of only one HIV-related risk factor exceeded 50%; tenofovir use was inversely associated with common cIMT. All other antiretroviral medications had posterior probabilities far below the 50% selection criterion. When we fit a model substituting the antiretroviral classes for the individual medications, the posterior probabilities for medication classes were all zero for common cIMT. For internal cIMT, only protease inhibitors (1.6%) and NNRTIs (2.5%) had a nonzero posterior probability. Posterior probabilities for the other covariates did not differ appreciably in this alternate model using classes instead of individual agents. None of the inflammatory markers had a posterior probability of greater than 4% in any BMA analysis for either common or internal cIMT.

Table 4 shows models for both carotid segments containing all variables that had a posterior probability of at least 50% in either segment. There were some noteworthy differences in the estimates of effect for predictive variables between the two cIMT regions (Table 4). Smoking, for example, was strongly predictive for internal cIMT but did not appear important for common cIMT. Similarly, BP was strongly predictive for common cIMT but was more weakly associated with internal cIMT in the BMA analysis. Of note, tenofovir was selected for the common carotid with a posterior probability of 51% and was associated with less thick common cIMT. Tenofovir was the only HIV-related factor that was selected for either region of the carotid artery (internal or common). We also observed an inverse association of duration of tenofovir use with internal cIMT (tenofovir association −0.018 mm/year of use) but it did not reach statistical significance, possibly due to the much higher variance in the internal cIMT effect [95% confidence interval (CI) −0.044 to 0.008].

Tenofovir users were very similar to nonusers with respect to demographic characteristics and most traditional cardiovascular risk factors. However, compared to nonusers, tenofovir users had lower total cholesterol levels ($P = 0.04$), lower CD4 nadir levels ($P < 0.01$) and were more likely to have a history of clinical AIDS ($P < 0.01$). There were no statistically significant differences between tenofovir users and nonusers in mean duration of HIV disease ($P = 0.10$) or in the proportion of participants with a detectable HIV viral load at the follow-up examination ($P = 0.92$). This low level of confounding by cardiovascular and HIV-related risk factors was supported by noting that the age- and sex-adjusted estimates of the association of tenofovir with common (−0.010 mm/year of use; 95% CI −0.019 to −0.001) and internal (−0.021 mm/year of use; 95% CI −0.046 to −0.0004) cIMT was close to the fully adjusted estimates.

As an additional sensitivity analysis, we added each candidate variable (from Table 3) to the final statistical model for common cIMT (Table 4) one at a time in order to directly test for any possible confounders that might have been overlooked by our primary modeling strategy. None of the variables, when introduced to the model, resulted in a change of greater than 7% for the point estimate of the association between tenofovir and common cIMT.

We also tested the effect of excluding lipids from the model. In BMA analysis that excluded lipids and diabetes, tenofovir was again selected (posterior probability of 51.2% for common cIMT), whereas no other antiretroviral drug showed greater than 50% posterior probability for internal or common cIMT. All had less than 25% posterior probability. In the multivariable model, excluding lipids and diabetes increased the strength of the association of tenofovir for both common cIMT (ΔcIMT = −0.0100, 95% CI −0.0184 to −0.0017; $P = 0.019$) and internal cIMT (ΔcIMT =−0.0198, 95% CI −0.0452 to 0.0057; $P=0.13$).

As an alternative sensitivity analysis, we examined models that defined common and internal cIMT as done in the ARIC study. For common cIMT, only age, African-American race and systolic BP had posterior probabilities greater than 50% (Supplemental Table 1, http://links.lww.com/QAD/A56). For internal cIMT, age, smoking, and systolic BP had posterior probabilities greater than 50%. Multivariable linear regression analysis of ARIC-defined IMT performed as described above showed similar results to our FRAM-defined IMT variables (Supplemental Table 2, http://links.lww.com/QAD/A57).

For common cIMT, some traditional risk factors were more strongly associated (African-American and smoking), whereas others were not as strongly associated (age, Hispanic, systolic BP, diastolic BP, and HDL) for ARIC-defined cIMT versus FRAM-defined cIMT. The tenofovir association remained protective but lost statistical significance. Likewise, for internal cIMT, results for ARIC-defined cIMT were generally consistent with FRAM-defined cIMT.

In analyses of plaque, as defined by cIMT greater than 1.5 mm, age, smoking and African-American race were selected by BMA (Supplemental Table 1, http://links.lww.com/QAD/A56). In multivariable analysis, age and smoking were associated with plaque, whereas African-American race was protective.

Discussion

In this cohort of HIV-infected participants, we did not find evidence of an association between markers of HIV disease severity or most antiretroviral drugs or classes and cIMT. However, we are not able to rule out modest effects of HIV-related factors with the data available as confidence intervals do include modest associations. Interestingly, the only HIV-related factor that was identified as being associated with cIMT using our BMA approach was the antiretroviral drug tenofovir, which was associated with lower cIMT. Our Bayesian model analysis found every other HIV-specific factor, as well as the three candidate inflammatory markers, to have a less than 20% chance of truly being predictive of higher cIMT. These results differ from some previous work in that no HIV-specific risk factor appeared likely to be related to increased atherosclerosis, although other reports have found results similar to ours [16]. Previous investigations have found HIV-specific factors such as a low CD4 cell count [17] and protease inhibitor use [7–8] to be associated with higher cIMT, although these have often been overshadowed by traditional risk factors [12]. Compared to participants included in many previous studies, those in FRAM have been HIV-infected for a much longer time; mean duration of known HIV infection at the time that cIMT was measured was 13 years (minimum 5.8 years). Risk factors identified in previous studies may be markers for pathologic pathways active earlier in the course of HIV disease; they may be much more difficult to identify in cohorts with longer durations of infection in which these processes are already completed. Baseline measures of cIMT before infection would be ideal to understand the contribution of HIV infection but are not feasible. Measures of IMT before treatment with antiretroviral therapy might prove helpful in understanding this process. It is also possible that we are not measuring important HIV-related factors associated with cIMT.

It is also possible that traditional cardiovascular risk factors are more important than measurable HIV-related factors as predictors of increased risk of atherosclerosis or vascular disease, particularly among individuals who have been HIV-infected and treated for many years. Published data indicate that the combined effect of all traditional CVD risk factors on cIMT are more important than the overall effect of HIV that would be a sum of all HIV-related factors [16]. For example, we reported that after adjusting for traditional CVD risk factors, the effect of HIV was similar to that of smoking, diabetes, or being 5–10 years

older. Thus although HIV represents a significant risk factor, its quantitative contribution does not appear to be dominant risk. Furthermore, if multiple HIV-related factors contribute to the overall HIV effect, it may prove difficult to quantify their individual contributions.

It is unclear whether tenofovir use has a causal link to cIMT. Our analysis found a modest probability of association, but even if the posterior probability were very high, we could not infer causality without additional evidence. One conjecture for the protective tenofovir effect is supported by the results of a small clinical trial that showed that addition of tenofovir to the treatment regimens of HIV-infected persons with suppressed viral loads on HAART lowered LDL cholesterol [32]. Additional data describes improvements in lipids among participants switched to tenofovir [33–36]. In our primary models, we controlled for current cholesterol using statistical adjustment. When we assessed the effect of tenofovir independent of lipids, the tenofovir effect strengthened. Tenofovir users in FRAM had worse HIV disease characteristics, which might suggest that tenofovir use could be acting as a marker for HIV disease severity, especially in patients with long-standing infection. However, the inverse association of tenofovir use with cIMT is counterintuitive, if tenofovir is a marker of disease severity, as Kaplan *et al.* [17] found that lower CD4 count was associated with increased atherosclerosis. Another possibility is that the tenofovir effect is related to the effects of antiretroviral therapy *per se*.

An alternative explanation for the association between tenofovir and cIMT is the possibility that tenofovir is acting as a marker for some patient characteristic that is also associated with the use of this agent. For example, it is plausible that stavudine may have been replaced with tenofovir in participants with a history of dyslipidaemia [33]. As antiretroviral medications are given in combination, the standard concerns about inference in correlated data apply here, although the Bayesian approach may mitigate some of these concerns [37]. Further research on the properties of tenofovir, especially randomized trials, will be required to see if this novel finding is replicated.

Study limitations include the use of cross-sectional data for risk factors and cIMT. We cannot rule out a small effect of factors with very low posterior probability, such as sex and diabetes. We found in previous work [6] that the increase in cIMT due to HIV infection was larger in women. This finding could explain why sex did not appear to be a risk factor in our HIV-infected cohort.

The FRAM cohort is broadly treated and all of the participants in this report were infected with HIV for more than 5 years and a median of 13 years. The FRAM population resembled that of HCSUS [23], which is representative of HIV infection in the US and therefore provides insight into CVD in developed nations. It is quite possible that we are unable to isolate any general effects of HIV or antiretroviral treatment on the increase in cIMT. In particular, if antiretroviral therapy as a broad, encompassing class of mediators had an overall effect of increasing cIMT, then it would be difficult to detect it in this study given the large proportion of treated participants and their long treatment histories. To examine this, we tested duration of HAART and found 0% probability by BMA analysis. In this context, it is important to note that the SMART study found fewer cardiovascular complications in those on continuous HAART compared to interrupted therapy [38]. Therefore, although we cannot definitively rule out an important contribution of antiretroviral drugs to the greater cIMT associated with HIV infection, it is plausible that other factors may be more important. Prospective studies may be better able to find effects of antiretroviral therapy.

More research is needed to understand the reasons why subclinical vascular disease appears to be accelerated among those with HIV infection. Although carotid IMT is an excellent

predictor of CVD, it does not address all mechanisms leading to myocardial infarction and stroke. For example, HIV infection and its therapies may affect the clotting cascade [39,40] leading to increased thrombosis with plaque rupture. The present cross-sectional examination of participant characteristics has not provided any clear hypotheses as to why those with HIV infection are at increased risk of developing vascular disease. However, our results are consistent with previous work that used the same methods, reading center, and approach [16] and with other studies that suggest that traditional risk factors are more important in predicting levels of cIMT in HIV infection. This may indicate that we need to examine HIV-infected cohorts at earlier stages of infection to understand the pathophysiology of vascular disease in those with HIV infection. Further prospective work will be required to understand this HIV-associated vascular disease.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1
Characteristics of the 538 HIV-infected participants

	All participants
Age at scan	48.0 [8.4]
Male	69%
African–American	41%
Hispanic	8%
Current smoker	36%
Past smoker	24%
Systolic blood pressure (mmHg)	124.6 [17.5]
Diastolic blood pressure (mmHg)	77.7 [10.2]
Antihypertensive use	30%
Total cholesterol (mg/dl)	186.6 [46.7]
HDL cholesterol (mg/dl)	45.8 [16.9]
LDL cholesterol (mg/dl)	102.0 [39.5]
Hypolipidemic use	25%
Diabetes	9%
Fasting glucose (mg/dl)	97.1 [27.0]
History of CAD	11%
Family history of CAD	
Parent	34%
Sibling	6%
C-reactive protein (mg/l)	4.26 [7.61]
Interleukin-6 (pg/ml)	2.51 [7.66]
Fibrinogen (mg/l)	394 [117]
Injection drug user	17%
Men who have sex with men	58%
AIDS by OI alone	53%
AIDS by CD4 and OI	77%
Known duration of HIV (years)	13.0 [4.1]
CD4 cell count (current) (cells/μl)	461 [279]
CD4 cell count (nadir) (cells/μl)	163 [166]
Undetectable HIV RNA	69%
HCV infection	23%
Common cIMT (mm)	0.88 [0.17]
Internal cIMT (mm)	1.16 [0.49]

Missing data handled by single imputation (<2% for any variable). Mean [standard deviation] or percentage. CAD, coronary artery disease; cIMT, carotid intimal–medial thickness; HCV, hepatitis C virus; HDL, high-density lipoprotein; HIV, human immunodeficiency virus; OI, opportunistic infection.

Table 2

Frequency and mean duration of antiretroviral medication use by HIV-infected participants (*n*=538)

ARV medication	Percentage of participants having ever taken ARV medication	Mean duration of use of ARV medication in users (years)
HAART	93.8	6.0
NRTI (all)	96.8	8.5
PI (all)	83.8	5.4
NNRTI (all)	70.3	3.6
Lamivudine	89.7	5.8
Zidovudine	80.2	4.6
Stavudine	63.7	4.0
Tenofovir	53.7	2.1
Didanosine	44.0	2.6
Abacavir	41.4	3.3
Emtricitabine	24.8	1.2
Zalcitabine	11.1	1.5
Ritonavir	58.0	3.6
Indinavir	43.5	3.3
Nelfinavir	40.0	2.9
Lopinavir	31.0	2.7
Saquinavir	27.3	3.7
Atazanavir	21.5	1.5
Amprenavir	9.3	1.9
Fosamprenavir	6.2	1.5
Darunavir	3.7	0.1
Tipranavir	0.5	0.4
Efavirenz	50.4	3.0
Nevirapine	29.1	3.2
Delavirdine	3.9	2.1
Entry inhibitors	3.7	1.4

ARV, antiretroviral; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; PI, protease inhibitor.

Table 3

Posterior probabilities for selection of predictive variables in a model for the association between participant characteristics and increased internal or common carotid intimal–medial thickness using Bayesian model averaging

Predictor	Common cIMT (%)	Internal cIMT (%)
Male	18.4	0
Age	100	100
African–American	100	0
Hispanic	50.8	3.6
Systolic blood pressure	97.4	8.8
Diastolic blood pressure	95.2	8.8
Current smoker	0	90.6
Past smoker	0	0
Diabetes	0	0
Total cholesterol	14.3	0
HDL cholesterol	84.9	5.8
Injection drug use	0	0
AIDS by OI alone	0	2.7
Duration of HIV infection	2.6	0
HCV infection	0	0
CD4 (baseline)	0.8	17.5
CD4 (nadir)	0	5.6
Undetectable viral load	1.8	9.9
C-reactive protein	0	3.1
Interleukin-6	0	0
Fibrinogen	0	0
Antiretroviral medications (duration of use)		
Lamivudine	0	0
Zidovudine	0	0
Stavudine	0	0
Tenofovir	51.3	3.3
Didanosine	0	0
Abacavir	0	0
Emtricitabine	0	0
Zalcitabine	0	0
Ritonavir	17.6	0
Indinavir	0	5.2
Nelfinavir	0	4.3
Lopinavir	0	0
Saquinavir	0	0
Atazanavir	0	0
Amprenavir	0	0
Fosamprenavir	5.0	0

Predictor	Common cIMT (%)	Internal cIMT (%)
Efavirenz	0	0
Nevaripine	0.9	0
Delavirdine	0	0

The results in this table are multivariate and reflect the weighted average of the probability that a variable will be included in one of the models with competitive goodness of fit. cIMT, carotid intimal–medial thickness; HCV, hepatitis C virus; HDL, high-density lipoprotein; OI, opportunistic infection.

Table 4

Estimates of the mean difference in common and internal carotid intimal–medial thickness associated with predictors

	Estimate (mm)	95% confidence limits	*P*
Common cIMT model			
Age (per 10 years)	0.097	0.080 to 0.114	<0.0001
African–American	0.059	0.034 to 0.085	<0.0001
Hispanic	0.069	0.027 to 0.112	0.0014
Current smoker	0.017	−0.007 to 0.041	0.17
Systolic blood pressure (per 10mmHg)	0.026	0.015 to 0.037	<0.0001
Diastolic blood pressure (per 10 mmHg)	−0.035	−0.055 to −0.016	0.0003
Tenofovir use (per year)	−0.009	−0.018 to −0.001	0.0278
HDL cholesterol (per 10mg/dl)	−0.011	−0.018 to −0.003	0.0038
Internal cIMT model			
Age (per 10 years)	0.263	0.209 to 0.317	<0.0001
African–American	−0.016	−0.095 to 0.063	0.69
Hispanic	0.077	−0.043 to 0.197	0.21
Current smoker	0.135	0.051 to 0.218	0.0016
Systolic blood pressure (per 10mmHg)	0.054	0.016 to 0.092	0.0051
Diastolic blood pressure (per 10 mmHg)	−0.085	−0.143 to −0.028	0.0035
Tenofovir use (per year)	−0.018	−0.044 to 0.008	0.17
HDL cholesterol (per 10mg/dl)	−0.02	−0.049 to 0.010	0.19

All variables with a posterior probability at least 50% for either internal or common cIMT are included in both. cIMT, carotid intimal–medial thickness; HDL, high-density lipoprotein.