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Correlates of hypertension in patients with AIDS in the era of highly-active antiretroviral therapy

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Abstract

Background—It is unclear whether HIV-related factors modify risk for hypertension (HTN). In a cohort of patients with AIDS, we determined HTN incidence and prevalence and assessed associated traditional, HIV-specific, and retinal vasculature factors.

Methods—Prospective observational cohort, 2,390 patients with AIDS (1998–2011). Univariate analysis was used to assess the impact of traditional and AIDS-related risk factors on HTN prevalence and incidence. Multivariate regression analyses were used to evaluate the adjusted impact of these factors.

Results—HTN prevalence was 22% (95% CI 21–24%) and was associated with traditional HTN risk factors (age, Black race, higher weight) as well as diabetes, hyperlipidemia, time since AIDS

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diagnosis and higher CD4+ T cell counts. HTN incidence was 64.1/1000 person-years (95% CI 58.7/1000 – 69.9/1000). Age, race, weight and diabetes were associated with incident HTN, but HIV-specific factors were not.

Conclusions—HTN, a prevalent cardiovascular risk factor in patients with AIDS, is associated with traditional and metabolic risk factors.

Keywords

AIDS; HIV; hypertension; cardiovascular risk; HAART

Introduction

In the era of highly-active antiretroviral therapy (HAART), chronic, non-infectious medical conditions, such as cardiovascular (CV) disease, are emerging as significant causes of morbidity and mortality among HIV-positive patients.(1–10) In this context, convincing evidence suggests that HAART should be prescribed for patients without interruption and at increasingly higher CD4+ T cell thresholds, despite its association with metabolic and CV risk and disease.(6, 11–17) Hypertension is among the traditional risk factors that contribute to CV disease in adults with HIV-infection.(18–20) The availability of effective anti-hypertensive medications allows the adverse consequences of hypertension to be mitigated.(21) Efforts to effect CV risk reduction in HIV-positive adults on antiretroviral therapy should therefore target hypertension as a known, modifiable risk factor.

To date, a small, diverse literature has identified traditional risk factors for hypertension in HIV-positive adults. These factors include older age, male sex, African-American race, higher body mass index (BMI) and elevated cholesterol.(22–24). These studies also associate several HIV-related factors with hypertension, including HAART initiation in treatment-naïve patients, duration of antiretroviral use, and longer time since HIV diagnosis.(22, 24) Inconsistent data exist about the effect of non-nucleoside reverse transcriptase inhibitors (NNRTIs) on hypertension in HIV-infected adults.(24–25) These studies encompass patients both with and without a diagnosis of AIDS. Because of the increased mortality risk of HIV-positive patients with AIDS, it is unclear whether these patients have the same risk of developing hypertension as do other HIV-positive patients.(26)

Clinical markers of hypertension are also important to identify in AIDS patients in order to determine hypertension risk and modify disease burden. Retinal vasculature provides a non-invasive source of end-organ information about cardiovascular changes associated with hypertension. In the general population, several studies have demonstrated an association between the development and progression of hypertension and narrower retinal arteriolar diameters.(27–31) An association between prevalent hypertension and baseline retinal vascular caliber among AIDS patients in the cohort examined in this study has been briefly described.(32) To our knowledge, no studies have examined the association between retinal arteriolar diameters and incident hypertension in patients with AIDS.

The aim of this study was to assess traditional, HIV-related, and retinal vascular factors associated with prevalent and incident hypertension in a large, prospective cohort of patients

with AIDS in the era of HAART. We hypothesized that traditional hypertension risk factors and duration of HIV-infection would be significantly associated with both prevalent and incident hypertension. We further hypothesized in secondary analysis of patients without a history of ocular opportunistic infections (OOI), that central retinal arteriolar equivalent (CRAE) narrowing would be associated with incident hypertension.

Methods

The Longitudinal Study of the Ocular Complications of AIDS (LSOCA) is a prospective observational study of patients with AIDS that began in September 1998. The study is designed to document the prevalence, incidence and course of AIDS-related ocular complications in the era of HAART. Eligible participants are ≥ 13 years of age and have an AIDS diagnosis according to the 1993 Centers for Disease Control and Prevention Case Surveillance definition of AIDS.(33)

Participant recruitment and study design have been described in detail elsewhere.(34–35) Briefly, recruitment was performed at 19 AIDS ophthalmology centers across the United States. Participants with or without opportunistic ocular infections and across a spectrum of immunologic function were included in the cohort on a rolling basis. The study and protocol were approved by institutional review boards at all participating centers and enrolled participants provided written informed consent.

At enrollment and follow-up, participants provided standardized medical histories to trained study personnel. According to study protocol, this data collection was primarily by self-report via interview, with review of participants' medical chart or contact of medical care providers, as necessary to clarify or confirm elements of the history. The medical history included details about HIV course, AIDS-related illnesses and antiretroviral therapy. Data on non-AIDS medical comorbidities (hypertension, diabetes, and hyperlipidemia) were also collected. Beginning in 2005, cigarette smoking and cardiovascular events were collected at baseline. Blood pressure medication use was recorded as of 2006.

Participants underwent baseline and follow-up ophthalmologic examination. Retinal photographs were taken on at study entry, every six months thereafter for participants with OOI, or every five years thereafter in participants without OOI. Retinal microvascular measurements and indices were determined in participants without OOI in a semi-automated manner by certified graders at the University of Wisconsin Fundus Photograph Reading Center (IVAN software, Department of Ophthalmology and Visual Science, University of Wisconsin, Madison, WI) using a standardized protocol, described previously.(36) These analyses resulted in two specific measurements of the retinal microvasculature: the projected caliber sizes of the central retinal artery (central retinal artery equivalent [CRAE]) and the central retinal vein (central retinal vein equivalent [CRVE]).(37–39)

Beginning in 2005, participants had direct weight and one-time height measurements recorded, with subsequent one-time body mass index (BMI) calculations. Also beginning in 2005, participants had direct blood pressure measurements. Using a standardized method, blood pressure was taken once in a seated position at each study encounter. Laboratory tests

performed at enrollment include CD4+ T cells and quantitative plasma HIV RNA levels (HIV viral load). Follow-up visits occur every three-to-six months for participants with an OOI, such as CMV retinitis, and every six months for those without an OOI.

Outcomes

Presence of hypertension was determined by data collected per study protocol during standardized baseline and follow-up medical history interviews, as described previously. A question was added to the medical history data collection forms September 30, 2005 specifically asking whether the patient was taking any hypertension treatments. Prior to that date, ascertainment of hypertensive treatment were obtained from an open-ended question asking about use of non-HIV/AIDS related treatments. Among 478 participants enrolled after September 30, 2005, 96% had agreement between their responses to taking any hypertension treatment and reported hypertension obtained during the study interview (kappa statistic = 0.90; 95% confidence interval [CI] 0.85 – 0.94). Because of this high agreement, the presence of hypertension was defined for all participants as either reported hypertension diagnosis or report of taking hypertensive treatment using the open-ended question. Participants who reported a history of high blood pressure requiring medication or reported taking any anti-hypertensive medications were therefore categorized as having prevalent disease. Those who reported neither at baseline, but did subsequently in follow-up, were coded as having incident hypertension. Given limited numbers, blood pressure measurements were not included in our outcome.

Predictors

The primary predictors of prevalent and incident hypertension were traditional hypertension risk factors (age, gender, and race, weight), baseline indicators of AIDS duration, severity and disease control (mean number of years since AIDS diagnosis, median CD4+T cell count, mean HIV viral load, median nadir CD4+ T cell count and mean peak HIV viral load), and HIV treatment history (HAART use and duration, protease inhibitor [PI] or non-nucleoside reverse transcriptase inhibitor [NNRTI] exposure at enrollment).

Secondary Analysis

To test our hypotheses about CRAE and hypertension, and to control for OOI effect on retinal vessels, we performed a secondary analysis in participants without a documented history of OOI. Models used in this analysis included the same variables used to assess hypertension incidence and prevalence in the general cohort, with the addition of CRAE and CVRE measurements as predictors.

Covariates

We adjusted all models for socio-demographic covariates, components of metabolic syndrome (hyperlipidemia and diabetes), CMV retinitis and hepatitis C co-infection.

Statistical Analyses

Data obtained and keyed into the database as of December 31, 2011 were included. Unadjusted associations of enrollment characteristics with prevalence of self-reported

hypertension or anti-hypertensive use were assessed using the t-test for unequal variance for continuous variables and the chi-square test for categorical variables. Multiple logistic regression was used to assess associations of participant enrollment characteristics with prevalence of reported hypertension or anti-hypertensive use. Collinearity was checked using variance inflation factors. Simple and multiple Cox regression were used to assess association of enrollment characteristics with incidence of reported hypertension or initiation of anti-hypertensive medications during follow-up among those without either at enrollment. Continuous covariates were modeled continuously except for retinal vascular measurements, which were modeled as quartiles. Because of the moderately large (12–14%) amount of missing data in the adjusted analysis, observations with missing HCV status were imputed as uninfected and observations with missing weight were imputed with the mean weight of 75 kg. Complete case analyses were similar. P-values were nominal, two-sided and were not adjusted for multiple outcomes or multiple looks. SAS 9.1 (SAS Institute, Cary, North Carolina) was used to analyze the data.

Results

As of December 31, 2011, there were 2,390 participants enrolled in LSOCA (Table 1). Overall, 80% of participants were male, 45% white, non-Hispanic, 37% Black, non-Hispanic, and 14% Hispanic. Approximately two-thirds of participants were 40–59 years old. Among all participants, 530 reported having high blood pressure requiring medication or reported using anti-hypertensive agents at enrollment, for a baseline hypertension prevalence of 22% (95% CI 21–24%, Table 2).

Prevalent Hypertension

In adjusted analysis, prevalent hypertension was associated with older age (OR 2.05 per 10 years of age, 95% CI 1.77–2.37, Table 3), Black race (OR 2.03, 95% CI 1.57–2.63), heavier weight (OR 1.21 per 10 kg, 95% CI 1.12–1.31) and lack of a college degree (OR for college graduation 0.74, 95% CI 0.57–0.98). Diabetes (OR 1.82, 95% CI 1.28–2.57) and hyperlipidemia (OR 2.18, 95% CI 1.66–2.87) were also significantly associated with hypertension. Subjects with prevalent hypertension had longer times since AIDS diagnoses (OR 1.04 per year, 95% CI 1.02–1.08) and higher CD4+ T cell counts (OR 1.09 per 100 cells/uL, 95% CI 1.02–1.16). HIV viral load (baseline and peak), nadir CD4+ T cell counts, HAART, antiretroviral class, hepatitis C co-infection and CMV retinitis were not significantly associated.

Incident Hypertension

The median follow up in this study was 6.5 years (0.1–13.3 years). Self-reported hypertension or initiation of anti-hypertensive medication in the LSOCA cohort was 64.1/1000 person-years (PY, 95% CI 58.7/1000 – 69.9/1000 PY, Table 4). In our adjusted model for incident hypertension among all participants, older age (hazard ratio [HR] 1.38 per 10 years, 95% CI 1.22–1.57, Table 5), Black race (HR 1.42, 95% CI 1.15–1.75), and higher weight (HR 1.18 per 10 kg, 95% CI 1.10–1.27) were associated with an increased risk. Diabetes (HR 1.97, 95% CI 1.45–2.67) was also associated with incident hypertension, whereas hyperlipidemia was not. Time since AIDS diagnosis, HIV viral load (baseline and

peak), CD4+ T cells (baseline and nadir), HAART use and antiretroviral class, CMV retinitis and hepatitis C co-infection were not significantly associated with incident hypertension in this model.

Secondary Analyses: Retinal microvasculature

The majority of participants (78%, Table 1) did not have OOI at enrollment. In unadjusted analysis of these participants, those with baseline hypertension had smaller mean CRAE measurements compared to participants without hypertension (OR 2.30, 1st vs. 4th quartile, 95% CI 1.55–3.43, Table 5), which remained significant in adjusted analysis (OR 2.16 1st vs. 4th quartile, 95% CI 1.23–3.78). In adjusted analyses, incident hypertension was also associated with smaller baseline CRAE (HR 2.87 1st vs. 4th quartile, 95% CI 1.86–4.42, Table 6). There were no significant associations between CRVE and either prevalent or incident hypertension.

Discussion

In this large, prospective study of patients with AIDS attending AIDS ophthalmology centers in the era of HAART, self-reported hypertension was present at enrollment in 22% of patients. Factors associated with prevalent hypertension were traditional hypertension risk factors and metabolic comorbidities (diabetes and hyperlipidemia), in addition to longer time since AIDS diagnosis and higher CD4+ T cells. Incident hypertension among participants was also associated with traditional risk factors and diabetes. In secondary analysis, narrower CRAE was associated with both prevalent and incident hypertension. These findings identify hypertension as a significant chronic condition in patients with AIDS. Furthermore, risk factors for hypertension in this population mirror those in the general population. The results of this study highlight the importance of screening for hypertension among patients with AIDS.

The prevalence of hypertension (22%) among LSOCA participants falls within the range identified in other studies of HIV-infected adults, and generally overlaps with prevalence in HIV-negative populations.(40–41) To our knowledge, only one other longitudinal study has described hypertension incidence among HIV-infected adults, and no other analyses are exclusively in subjects with AIDS. The Data Collection of Adverse Events of anti-HIV Drugs Study (D:A:D) reported hypertension incidence of 72.1/1000 PY (95% CI: 68.2–76.0).(24) This rate is similar to that in LSOCA, which was 64/1000 PY (95% CI 58.7/1000 – 69.9/1000 PY), with overlapping confidence intervals. The D:A:D study outcomes included measured blood pressure, compared to our largely self-reported outcome, which may, in part, explain the small variation in raw incidence rates between these two studies.

Traditional risk factors for hypertension in HIV-negative adults are well-established, and include Black race, hyperlipidemia, obesity, and age (21, 42–44). Our study confirms these factors are also associated with hypertension in patients with AIDS. Numerous public health interventions target hypertension prevention for the general population, and the overlap of hypertension risk factors in patients with AIDS and HIV-negative patients suggests that these interventions are applicable to this population as well.(21, 45) In addition, HIV-related factors have previously been associated with hypertension, including indicators of infection

duration.(22) A variety of studies suggest effects of chronic inflammation on endothelial function, the cardiovascular system and potentially on cardiovascular risk in individuals with HIV, regardless of viral suppression.(46–48) Presumably, the longer the duration of HIV infection, the greater the risk of lasting endovascular damage that might result in hypertension. The discrete mechanisms underlying these processes in HIV infection is an ongoing area of investigation, but their relationship to cardiovascular comorbidities remains important.(49) In this study, we also found an association between prevalent hypertension and time since AIDS diagnosis. Time since AIDS diagnosis may be considered a marker of overall infection duration, and suggests that a potential HIV-specific mechanism for hypertension in our participants might also be related to chronic inflammation. In addition, baseline CD4+ T cell counts were higher in participants with prevalent hypertension. This finding might also suggest that participants with more functional immune systems, and potentially greater inflammatory responses, might experience long-term vascular effects of chronic inflammation. Finally, central retinal microvasculature has been identified as a predictor of incident hypertension in the general population.(27, 29–31) In our study, narrower CRAE measurements were also associated with incident hypertension in AIDS patients without OOI. CRAE narrowing has been associated with cardiovascular risk and morbidity in certain groups of HIV-negative adults, as well as with mortality in AIDS patients.(27, 32, 50) Further work might elucidate the mechanisms underlying this relationship in the context of exposure to prolonged inflammation.

Longitudinal analysis of the D:A:D study data demonstrated a decreased risk of incident hypertension with cumulative exposure to NNRTIs.(24) In a smaller, cross-sectional study of patients attending a sexual health clinic in London, Wilson et al. found an association between NNRTI use and increased blood pressure.(25) In our study, neither HAART nor NNRTI-based HAART use at enrollment were associated with either prevalent or incident hypertension, further suggesting that HIV treatment may not, in and of itself, contribute to hypertension.

While our data were collected from a cohort with a primary aim of assessing ocular complications in AIDS patients, since its inception, LSOCA has been designed to additionally assess non-ocular outcomes, including mortality and visceral CMV. Furthermore, LSOCA enrollment included participants both with (22%) and without (78%) a history of OOI, and we found no increased risk of prevalent or incident hypertension in patients with CMV retinitis, the nearly exclusive form of OOI, compared to those without it.

Several additional limitations of this study merit comment. First, we do not have specific information on the degree to which reported diagnoses were additionally confirmed by study personnel via chart review and/or medical providers (as was possible given study protocol). A conservative approach, therefore, would be to assume that hypertension was largely self-reported and therefore subject to recall bias.

Second, our final analysis did not exclude participants who were on anti-hypertensive agents, did not explicitly report a diagnosis of hypertension, but were determined to have another diagnosis for which an anti-hypertensive agent might be prescribed (for example: beta-blockers in patients with coronary artery disease). We did perform a sensitivity analysis

using only reported hypertension as the outcome, excluding reported anti-hypertensive medication use. In this analysis, baseline differences between subjects with and without hypertension were similar compared to the final analysis reported in the results of this study. The prevalence of a reported hypertension diagnosis was 19% (vs. 22% in our final composite diagnosis and medication outcome). Hypertension incidence rate using only reported hypertension was lower (26/1000 PYs vs. 64/1000 PYs), suggesting that some of the hypertension incidence we report with our composite outcome may be due to anti-hypertensive medication use for other indications. Factors associated with prevalent and incident hypertension remained largely the same, with the exception of borderline significant associations between prevalent hypertension and baseline PI exposure (OR: 1.06, 95% CI 0.60–0.97); and incident reported diagnosis of hypertension and shorter time since AIDS diagnosis (OR: 0.94, 95% CI 0.90–0.98), as well as lower peak HIV viral load (OR: 0.86, 95% CI: 0.76–0.98).

Finally, we did not have sufficient observations on smoking status or BMI to include them in our regression models. In adjusted analyses, however, we demonstrated an association between heavier weight and hypertension.

Cardiovascular disease poses a comorbid burden to HIV-infected adults on HAART and likely results from a variety of factors, including aging, traditional risk factors, HIV itself, and medications.(13–17, 51) Convincing evidence relates continuous, early initiation of HAART to better outcomes, and therefore, the benefits of HAART outweigh the costs related to its role in comorbid disease development.(11–12, 19) Furthermore, effects of chronic inflammation may persist despite appropriate HIV control with HAART, resulting in ongoing cardiovascular disease risk.(49) Identifying components of cardiovascular risk and disease that are modifiable is therefore of increasing importance for patients with HIV and AIDS. Diagnosis and control of hypertension in general has been demonstrated as essential to improving cardiovascular disease outcomes.(21) Our study demonstrates that hypertension is a prevalent comorbidity in AIDS patients in the era of HAART, and suggests the value of screening for hypertension as a potential means to decreasing cardiovascular risk in this population.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Characteristics of overall study population, Longitudinal Study of the Ocular Complications of AIDS (LSOCA), as of December 31, 2011 (n=2,390)

Characteristic	%	n
Age, years		
13–17	<1	8
18–39	34	820
40–59	62	1476
60+	4	86
Male	80	1922
Race/Ethnicity		
White, non-Hispanic	45	1082
Black, non-Hispanic	37	876
Hispanic	14	339
Other	4	93
No Ocular Opportunistic Infection	78	1856

Table 2

Baseline characteristics of AIDS Patients with and without reported hypertension or use of hypertension treatment, as of December 31, 2011

		Reported HTN or Treatment		
	Total (n=2390)	**No (n=1860)**	**Yes (n=530)**	**P-value**
Demographics				
Age – y, Mean (SD)	43 (9)	42 (8)	48 (9)	<0.0001
Male, %	80	80	81	0.55
Black, %	37	34	46	<0.0001
College graduate, %	30	30	30	0.97
Insurance, %				<0.0001
Uninsured	16	18	10	
Publically insured	53	51	61	
Privately insured	31	32	29	
Unemployed, %	13	13	12	0.83
Weight – kg, Mean (SD)	75 (15)	74 (14)	79 (16)	<0.0001
HIV Characteristics and Treatment				
HIV Risk Factor, %*				0.27
MSM only	56	56	55	
IDU only	9	9	9	
MSM and IDU	4	4	5	
Heterosexual	26	27	24	
Time since AIDS diagnosis – y, Mean (SD)	4.9 (4.0)	4.6 (3.8)	6.0 (4.3)	<0.0001
CD4+ T-cells/μL, Median (pSD)	179 (205)	164 (200)	227 (233)	<0.0001
Nadir CD4+ T-cells/μL, Median (pSD)	30 (59)	27 (56)	34 (67)	0.02
Viral load – log copies/mL, Mean (SD)	3.2 (1.6)	3.2 (1.6)	3.0 (1.5)	0.0008
Peak viral load – log copies/mL, Mean (SD)	5.1 (1.0)	5.1 (0.9)	5.0 (1.1)	0.02
HAART use, %	84	83	86	0.10
PI-based HAART, %	63	63	61	0.46
NNRTI-based HAART, %	38	37	42	0.05
Comorbidities				
CMV retinitis, %	21	22	17	0.01
Hyperlipidemia, %	20	16	34	<0.0001
Diabetes, %	9	6	18	<0.0001
Hepatitis C virus, %				0.03
Uninfected	79	80	74	
Cleared	4	4	6	
Chronic	17	16	20	
Central Retinal Vasculature - μm, Mean, (SD)**	(n=1396)	(n=1103)	(n=293)	
CRAE	148 (16)	149 (16)	143 (15)	<0.0001

		Reported HTN or Treatment		
	Total (n=2390)	**No (n=1860)**	**Yes (n=530)**	**P-value**
CRVE	223 (25)	224 (25)	221 (25)	0.13

22% (95% CI 21–24%) of participants had hypertension at enrollment.

* Percents do not add to 100; category of “other” not included.

** n excludes participants with ocular opportunistic infections.

HTN: hypertension, MSM: men who have sex with men, IDU: injection drug use, HAART: highly-active antiretroviral therapy, PI: protease inhibitor, NNRTI: non-nucleoside reverse transcriptase inhibitor, CMV: cytomegalovirus, CRAE: central retinal artery equivalent, CRVE: central retinal vein equivalent

Table 3

Unadjusted and adjusted associations between enrollment characteristics and prevalent reported hypertension or use of hypertensive treatment at baseline*

	Unadjusted		Adjusted	
	Odds Ratio	**(95% CI)**	**Odds Ratio**	**(95% CI)**
Demographics				
Age (per 10 years)	2.24	(1.98 – 2.53)	2.05	(1.77 – 2.37)
Male	1.08	(0.84 – 1.38)	1.20	(0.85 – 1.70)
Black	1.68	(1.38 – 2.04)	2.03	(1.57 – 2.63)
College graduate	1.00	(0.81 – 1.24)	0.74	(0.57 – 0.98)
Uninsured	0.51	(0.37 – 0.69)	0.71	(0.49 – 1.02)
Unemployed	0.97	(0.72 – 1.30)	1.26	(0.88 – 1.80)
Weight (per 10 kg)	1.27	(1.19 – 1.36)	1.21	(1.12 – 1.31)
HIV Characteristics and Treatment				
HIV Risk Factor, MSM	1.01	(0.94 – 1.08)	1.02	(0.93 – 1.13)
Time since AIDS diagnosis (per year)	1.08	(1.06 – 1.11)	1.04	(1.02 – 1.08)
CD4+ T-cells (100 cells/μL)	1.14	(1.09 – 1.18)	1.09	(1.02 – 1.16)
Nadir CD4+ T-cells (100 cells/μL)	1.13	(1.00 – 1.27)	0.86	(0.72 – 1.03)
Viral load (log copies/mL)	0.90	(0.84 – 0.96)	1.07	(0.98 – 1.17)
Peak viral load (log copies/mL)	0.88	(0.80 – 0.98)	0.95	(0.84 – 1.07)
HAART	1.26	(0.96 – 1.66)	0.98	(0.66 – 1.46)
PI-based HAART	0.93	(0.76 - 1.13)	0.78	(0.58 – 1.04)
NNRTI-based HAART	1.22	(1.00 – 1.48)	1.12	(0.84 – 1.47)
Comorbidities				
CMV retinitis	0.72	(0.56 – 0.92)	0.93	(0.68 – 1.27)
Hyperlipidemia	2.70	(2.17 – 3.37)	2.18	(1.66 – 2.87)
Diabetes	3.09	(2.31 – 4.13)	1.82	(1.28 – 2.57)
Hepatitis C virus				
Cleared	1.50	(0.94 – 2.40)	1.19	(0.69 – 2.07)
Chronic	1.34	(1.03 – 1.76)	1.04	(0.75 – 1.44)

* n = 2,390 participants. There were 2,104 complete cases. 12% of data with missing weights imputed with average weight (75 kg) and 14% of data with missing HCV determinations imputed as uninfected.

MSM: men who have sex with men, IDU: injection drug use, HAART: highly-active antiretroviral therapy, PI: protease inhibitor, NNRTI: non-nucleoside reverse transcriptase inhibitor, CMV: cytomegalovirus

Table 4

Unadjusted and adjusted associations between enrollment characteristics and incident reported hypertension or use of hypertensive treatment among, participants without ocular opportunistic infections*

	Unadjusted		Adjusted	
	Hazard Ratio	**(95% CI)**	**Hazard Ratio**	**(95% CI)**
Demographics				
Age (per 10 years)	1.38	(1.24 – 1.53)	1.38	(1.22 – 1.57)
Male	0.96	(0.77 – 1.20)	0.82	(0.62 – 1.09)
Black	1.31	(1.10 – 1.57)	1.42	(1.15 – 1.75)
College graduate	0.96	(0.80 – 1.16)	0.96	(0.76 – 1.19)
Uninsured	0.90	(0.71 – 1.14)	1.02	(0.78 – 1.33)
Unemployed	1.24	(0.96 – 1.61)	1.27	(0.95 – 1.71)
Weight (per 10 kg)	1.16	(1.09 – 1.23)	1.18	(1.10 – 1.27)
HIV Characteristics and Treatment				
HIV Risk Factor, MSM	1.02	(0.96 – 1.08)	1.00	(0.92 – 1.09)
Time since AIDS diagnosis (per year)	1.02	(1.00 – 1.05)	1.00	(0.98 – 1.03)
CD4+ T-cells (100 cells/μL)	1.00	(0.96 – 1.04)	0.97	(0.92 – 1.02)
Nadir CD4+ T-cells (100 cells/μL)	0.96	(0.85 – 1.07)	0.95	(0.82 – 1.10)
Viral load (log copies/mL)	1.00	(0.94 – 1.06)	1.02	(0.95 – 1.09)
Peak viral load (log copies/mL)	0.96	(0.88 – 1.06)	0.98	(0.88 – 1.08)
HAART	1.03	(0.81 – 1.32)	1.01	(0.73 – 1.41)
PI-based HAART	1.22	(1.01 – 1.47)	1.11	(0.86 – 1.43)
NNRTI-based HAART	0.88	(0.74 – 1.06)	0.94	(0.75 – 1.17)
Comorbidities				
CMV retinitis	1.06	(0.86 – 1.30)	1.20	(0.95 – 1.51)
Hyperlipidemia	1.23	(1.00 – 1.06)	1.13	(0.88 – 1.44)
Diabetes	2.24	(1.70 – 2.96)	1.97	(1.45 – 2.67)
Hepatitis C virus				
Cleared	1.27	(0.84 – 1.92)	1.07	(0.69 – 1.64)
Chronic	1.38	(1.08 – 1.76)	1.14	(0.86 – 1.51)

Hypertension incidence was 64.1/1000 person-years (95% CI 58.7/1000 – 69.9/1000 PY)

* n = 1,783 participants without baseline hypertension and with available follow-up data. All variables selected for multiple Cox regression model. There were 1,576 complete cases. 12% of data with missing weights imputed with average weight (75 kg) and 15% of data with missing HCV determinations imputed as uninfected.

MSM: men who have sex with men, IDU: injection drug use, HAART: highly-active antiretroviral therapy, PI: protease inhibitor, NNRTI: non-nucleoside reverse transcriptase inhibitor, CMV: cytomegalovirus

Table 5

Unadjusted and adjusted associations between retinal vasculature measurements and prevalent reported hypertension or use of hypertensive treatment at baseline, participants without ocular opportunistic infections*

	Unadjusted		Adjusted**	
	Odds Ratio	**(95% CI)**	**Odds Ratio**	**(95% CI)**
Central Retinal Artery Equivalent				
1st vs. 4th quartile	2.30	(1.55 – 3.43)	2.16	(1.23 – 3.78)
2nd vs. 4th quartile	1.80	(1.20 – 2.69)	1.89	(1.14 – 3.15)
3rd vs. 4th quartile	1.33	(0.87 – 2.03)	1.08	(0.65 – 1.78)
Central Retinal Vein Equivalent				
1st vs. 4th quartile	1.48	(1.00 – 2.19)	1.18	(0.68 – 2.07)
2nd vs. 4th quartile	1.36	(0.92 – 2.02)	1.11	(0.66 – 1.85)
3rd vs. 4th quartile	1.36	(0.92 – 2.02)	1.52	(0.94 – 2.47)

* n = 1,255 participants without ocular opportunistic infection and with available retinal vasculature measurements

** Adjusted for demographics (age, sex, race, education, insurance status, employment status, weight), HIV characteristics and treatment (HIV risk factor. Time since AIDS diagnosis, CD4+ T-cells: baseline and nadir, HIV viral load: baseline and peak, HAART, PI-based HAART, NNRTI-based HAART) and comorbidities (hyperlipdemia, diabetes and hepatitis C infection: cleared and chronic)

Table 6

Unadjusted and adjusted associations between retinal vasculature measurements and incident reported hypertension or use of hypertensive treatment at baseline, participants without ocular opportunistic infections*

	Unadjusted		Adjusted**	
	Hazard Ratio	**(95% CI)**	**Hazard Ratio**	**(95% CI)**
Central Retinal Artery Equivalent				
1st vs. 4th quartile	2.28	(1.63 – 3.21)	2.87	(1.86 – 4.42)
2nd vs. 4th quartile	1.53	(1.07 – 2.17)	2.06	(1.36 – 3.13)
3rd vs. 4th quartile	1.56	(1.09 – 2.22)	1.73	(1.17 – 2.57)
Central Retinal Vein Equivalent				
1st vs. 4th quartile	1.11	(0.81 – 1.52)	0.80	(0.53 – 1.21)
2nd vs. 4th quartile	0.94	(0.68 – 1.31)	0.83	(0.56 – 1.22)
3rd vs. 4th quartile	0.87	(0.62 – 1.21)	0.83	(0.57 – 1.22)

* n = 938 participants without ocular opportunistic infection or baseline hypertension and with available retinal vasculature measurements

** Adjusted for demographics (age, sex, race, education, insurance status, employment status, weight), HIV characteristics and treatment (HIV risk factor. Time since AIDS diagnosis, CD4+ T-cells: baseline and nadir, HIV viral load: baseline and peak, HAART, PI-based HAART, NNRTI-based HAART) and comorbidities (hyperlipdemia, diabetes and hepatitis C infection: cleared and chronic)