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Contributions of HIV, HCV, and Traditional Vascular Risk Factors to Peripheral Artery Disease in Women

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Abstract

Objectives: Human immunodeficiency virus (HIV) and hepatitis C virus (HCV) have been associated with cardiovascular disease (CVD), but it is unclear whether HIV and HCV are also associated with peripheral artery disease (PAD). We examined the association of HIV, HCV, and traditional CVD risk factors with PAD in the Women's Interagency HIV Study (WIHS), a multicenter U.S. cohort.

Methods: In this cross-sectional study, ankle-brachial index (ABI) was estimated using Doppler ultrasound and manual sphygmomanometer in 1,899 participants aged >40 years with HIV/HCV coinfection, HCV or HIV monoinfection, or neither infection. Multivariable logistic regression was used to estimate the odds of PAD (ABI≤0.9) after controlling for demographic, behavioral, and CVD risk factors.

Results: Over two-thirds were African-American, median age was 50 years, and PAD prevalence was 7.7% with little difference by infection status. After multivariable adjustment, neither HIV nor HCV infection was associated with greater odds of PAD. Factors associated with PAD included older age [adjusted odds ratio (aOR): 2.01 for age 61-70 vs. 40-50 years; 95% confidence interval (CI): 1.04, 3.87], Black race (aOR: 2.30; 95% CI: 1.15, 4.63), smoking (aOR: 1.27 per 10-pack-year increment; 95% CI: 1.09, 1.48), and higher SBP (aOR: 1.14 per 10 mmHg; 95% CI: 1.01, 1.28).

Conclusions: The high PAD prevalence in this nationally representative cohort of women with or at risk for HIV is on par with general population studies in individuals a decade older than our study’s median age. HIV and HCV infection are not associated with greater PAD risk relative to uninfected women with similar risk factors. Modifiable traditional CVD risk factors may be important early intervention targets in women with and at risk for HIV.

Keywords

HIV; Hepatitis C; Peripheral Arterial Disease; Women; Ankle Brachial Index

Introduction

Cardiovascular disease (CVD) is now one of the most common causes of death among persons living with HIV (PLWH) in the U.S.[1] In addition to traditional vascular risk factors, the increased CVD risk in PLWH may be related in part to chronic inflammation that persists even with HIV suppression.[2-5] As a result, some have suggested that PLWH may be at increased risk for other manifestations of atherosclerosis, including peripheral artery disease (PAD).[6-8] Cigarette smoking, which is common in PLWH, is consistently reported as a strong risk factor for PAD in the general population.[9, 10] Furthermore, PAD itself is associated with decline in physical function, limb amputation, other major vascular

events (including myocardial infarction), and mortality in the general population.[11-17] Taken together, PAD may be a significant clinical problem in PLWH.

Few studies have adequately examined the association of HIV with PAD; most were limited by small sample sizes, rarely included an HIV-seronegative comparison group, and were conducted mainly in men.[6, 7, 16, 18-25] Even fewer studies have examined the association of hepatitis C virus (HCV) with PAD. One large study in mostly men from the Veterans Administration Cohort Study (VACS) examined the association of HIV and HCV infection and found that HIV and HCV were independently associated with a greater incidence of PAD diagnosis based on ICD-9 and CPT codes in electronic health records.[25] However, only 11% of patients with PAD have classic symptoms of claudication and many PAD cases are undiagnosed.[26] Therefore, it is unclear whether the findings from VACS can be generalized to PAD according to the first-line measure for PAD diagnosis, the ankle-brachial index (ABI).

Population-based studies suggest that the prevalence of PAD as measured by ABI is higher in women than in men, and higher in African-Americans than in Caucasians.[27, 28] Women with PAD may also have greater walking impairment from leg symptoms, greater leg pain with exertion and rest, critical limb ischemia, and faster rates of functional decline when compared to men with PAD.[28-30] A recent large study from Copenhagen in mostly men of European ancestry found that HIV infection was associated with a greater risk of PAD as measured using the ABI when compared to a large population-based cohort of HIV-seronegative controls[31]. In an earlier analysis from a small subset of HIV seropositive and seronegative women with a median age under 40 years, there was an unexpectedly high prevalence (6.9%) of ABI values >1.4 which is suggestive of arterial calcification that showed little difference by HIV status. This small study did not use the gold standard Doppler-based ABI.[22] Whether HIV relates to PAD risk in women needs study in a larger, well-phenotyped cohort.

We therefore examined potential associations of HIV, HCV, and traditional CVD risk factors with PAD in a large, ethnically and geographically diverse cohort of women with or at risk for HIV. PAD was determined via the clinical gold standard ABI measurement.

Methods

Setting and participants

The WIHS is a multi-center prospective cohort study of women with and without HIV infection that enrolled a total of 4,982 women (3,678 HIV-seropositive and 1,304 HIV-seronegative but at risk for HIV infection). Enrollment occurred during four recruitment waves: 1994-1995, 2001-2002, 2011-2012, and 2013-2015 from 10 U.S. cities (Bronx and Brooklyn, NY; Chicago, IL; San Francisco, CA; Los Angeles, CA; Washington D.C.; Atlanta, GA; Chapel Hill, NC; Miami, FL; Jackson, MS; and Birmingham, AL). Full details of recruitment, retention, and demographics have been published previously.[32-34] Baseline sociodemographic characteristics and HIV risk factors were similar between HIV-seropositive and HIV-seronegative women. Each WIHS site's institutional review board approved the study protocol and consent form, and each participant gave written informed

consent. At semi-annual research visits, participants completed a brief physical examination, provided biological specimens, and completed an interviewer-administered questionnaire.

PAD determination

In this cross-sectional study, we measured ABI in 1,917 WIHS participants aged greater than 40 during exams conducted between October 2013 and March 2016. Prior to the ABI procedure, the right mid-arm circumference was measured to determine appropriate arm cuff size. Blood pressure cuffs were placed on both arms and both legs. The participant lay supine on a flat examination table for five minutes prior to the exam. Single measures of systolic blood pressure were measured utilizing a hand-held Doppler instrument with a 5mm Hz probe and an aneroid sphygmomanometer at the brachial artery on both arms and the dorsalis pedis and posterior tibial arteries on both legs. All technicians were trained and certified by the same primary study technician after practicing on an average of 15 volunteers.

ABI was calculated for the left and the right limbs by dividing the higher pressure of the lower extremity arterial measurements for each side by the higher pressure of either the left or right brachial artery. The lower of the two ABI values (right versus left) was used for analysis. This method is consistent with the American Heart Association (AHA)/American College of Cardiology (ACC) Guidelines for measurement of ABI.[35] PAD was defined as an abnormal ABI ≤0.9 as per the 2016 AHA/ACC Guidelines.[35, 36] Participants with non-compressible vessels (ABI>1.4) (n=8) and unknown HCV status (n=10) were excluded from the analysis, leaving a total of 1,899 women.

Predictors and Covariates

Our primary predictors were HIV and HCV status. We confirmed HIV status with an FDA-approved ELISA and re-confirmed with a Western blot assay when immunosorbent assays were positive. Chronic HCV status was confirmed by detectable HCV RNA following a positive anti-HCV antibody result at the time of enrollment into WIHS and if treated, by detectable HCV RNA at least six months after HCV treatment completion. Of the participants included in the analysis with HCV infection at the time of enrollment into the WIHS PAD Substudy, about one-quarter reported undergoing HCV treatment. About 80% of those reporting HCV treatment had available data on a sustained virologic response (SVR), i.e. undetectable HCV RNA more than six months after completing HCV treatment, of whom <20% achieved an SVR and were categorized as not having chronic HCV infection in the ABI analysis. Women with missing HCV RNA data were categorized as having chronic HCV infection.

Other candidate covariates included participant sociodemographics (i.e., age at the time of ABI measurement, sex and race/ethnicity) and behavioral factors [i.e., self-reported alcohol use (none; light drinking 1-15 gm/day; moderate drinking 15-30 gm/day; heavy drinking >30 gm/day) and self-reported smoking history (categorized as none, current, past) and quantity of pack-years of smoking], anthropometric measures (i.e., waist circumference), body mass index [BMI], insulin resistance quantified using the Homeostasis Model Assessment (HOMA) defined as fasting insulin (μU/mL) × glucose (mg/dL)/405, diabetes

mellitus (DM) (defined by: 1] report of anti-DM medication, 2] having an elevated fasting glucose (FG) ≥126mg/dL confirmed by a subsequent FG≥126mg/dL, report of anti-DM medication, or a confirmed hemoglobin A1C (A1C) value ≥6.5%; and 3] a report of DM confirmed by a subsequent report of anti-DM medication or two FG measurements ≥126mg/dL, or FG≥126mg/dL concurrent with A1C≥6.5%), systolic and diastolic blood pressure, pulse pressure, and laboratory parameters, including estimated glomerular filtration rate and lipid measurements. Liver fibrosis severity was also calculated using the aspartate aminotransferase to platelet ratio index (AST/upper limit of normal AST)*100/platelet count). In HIV-seropositive participants, HIV-related parameters included current CD4 cell count, CD4 cell count nadir, current HIV RNA level, history of clinical AIDS and current use of antiretroviral therapy (ART).

Statistical analysis

We first compared sociodemographic and clinical characteristics across 4 infection groups: those with HIV/HCV coinfection, HCV monoinfection, HIV monoinfection, and neither HIV nor HCV infection. For continuous variables, we compared characteristics using ANOVA for normally distributed variables and the Kruskal-Wallis test for non-normally distributed variables. We used the chi-squared test or Fisher exact test for categorical variables,

We first used unadjusted logistic regression analysis to model associations of infection status and other risk factors with odds of PAD. Staged models were then used to adjust sequentially for: 1) demographic factors; 2) demographic and behavioral factors; 3) demographic, behavioral, and CVD risk factors; and 4) demographic, behavioral, and CVD risk factors, and liver fibrosis. Stratified logistic regression models were used to examine the associations between each of the potential predictors and PAD within each infection group or within the entire cohort, while controlling for all other potential confounders. Type III analysis based on saturated generalized linear model with binary outcome was performed and F-statistic based on mean sum of squares and residual sum of squares was used to test the overall interaction effect between each individual covariate and disease strata. We further used backward stepwise logistic regression analysis to construct parsimonious multivariable models to determine the significant factors affecting PAD while controlling for demographic factors and infection status. In models with ~25% missing metabolic data, multiple imputation with the Markov chain Monte Carlo method was used to impute missing values, with 25 repetitions.[37, 38] All analyses were performed using SAS system, version 9.4 (SAS Institute Inc., Cary, NC).

Results

Characteristics of the study population

Table 1 shows the demographic and clinical characteristics of the 1,899 women included in the analysis by HIV and HCV infection status. Over half (57%) had HIV monoinfection, 15% HIV/HCV coinfection, 5% HCV monoinfection, and 22% neither HIV nor HCV infection. Over two-thirds of the cohort was African American. Women with HCV infection were older (median age 54-55 vs 49-50 years for women without HCV infection), more

commonly post-menopausal, and more likely to report smoking cigarettes than women with HIV monoinfection and those with neither HIV nor HCV infection. Overall, there was a high prevalence of hypertension (>50%), diabetes (21-33%), current smoking (73% in those with HCV monoinfection, 35% in those with HIV monoinfection), and overweight/obesity across all infection groups. Among women with HIV infection, the majority were taking ART and had an undetectable HIV RNA level (≤20) and a CD4 T cell count >500 cells/mm^3.

In the entire cohort, 7.7% of women had PAD. The prevalence of PAD by infection status was 10% in those with HIV/HCV coinfection, 5.3% in those with HCV monoinfection, 7.5% in those with HIV monoinfection, and 7.2% in those with neither HIV nor HCV infection (Figure 1a). In unadjusted models, the odds of PAD were highest in those with HIV/HCV coinfection (odds ratio [OR]: 1.41 [95% CI: 0.83, 2.39] and lowest in those with HCV monoinfection (OR: 0.71 [95% CI:0.27,1.89]) relative to those with neither HIV nor HCV infection, but differences did not reach statistical significance (Figure 1b).

Association of HIV and HCV infection with PAD

We then conducted multivariable logistic regression analysis to determine whether HIV and HCV infection were associated with PAD, independent of possible confounders. In demographic-adjusted analysis, the odds of PAD were 13% *higher* in those with HIV/HCV coinfection and 39% *lower* in those with HCV monoinfection relative to those with neither HIV nor HCV infection, but differences did not reach statistical significance (Table 2). There was little change in these relative differences after further adjustment for behavioral and CVD risk factors, and liver fibrosis. HCV monoinfection remained associated with lower odds of PAD at all levels of adjustment, but did not reach statistical significance. At all levels of adjustment, HIV monoinfection showed similar odds of PAD relative to those with neither HIV nor HCV infection.

Association of demographic, behavioral, and vascular risk factors with PAD

Table 3 shows the factors associated with PAD in univariable and parsimonious multivariable analysis of the whole cohort. In unadjusted models, older age (ages 51-60 and 61-70 years in comparison to ages 40-50 years), longer pack-year history of smoking, greater waist circumference, diabetes, higher triglyceride level, higher LDL level, current statin use, and higher systolic blood pressure were significantly associated with higher odds of PAD. After multivariable adjustment, older age (61-70 vs. 40-50 years), longer pack-year smoking history, and higher systolic blood pressure remained associated with PAD. The association of waist circumference with PAD was slightly attenuated and did not reach statistical significance. The association of African-American race with PAD was strengthened in multivariable analysis. In unadjusted models, we also found that the overall Atherosclerotic Cardiovascular Disease (ASCVD) risk score was associated with increased odds of PAD (OR:1.04 [95% CI:1.02-1.05]).

HIV infection (in the absence of presence of HCV infection) and HCV infection (in the absence or presence of HIV infection) were not associated with PAD in univariable or multivariable analysis. Interactions between each covariate (including CD4 count

stratification by CD4 <500 vs ≥500) and infection group were not significant (all p-values >0.05, data not shown). Among HIV-seropositive women, neither lower CD4 count nor detectable HIV viral load were associated with PAD (OR: 0.99 [95% CI:0.96,1.02] and 1.33 [95% CI:0.85,2.04], respectively) in adjusted models. Antiretroviral therapy (ART) use, including specific ART classes such as protease inhibitors, was not associated with PAD (data not shown).

Discussion

We report a high PAD prevalence ranging from 5-10% in our large cohort of predominantly middle-aged African-American women with and at risk for HIV and/or HCV infection. Contrary to our expectations, we did not observe an evident association of HIV and HCV infection with PAD compared to those with neither HIV nor HCV infection. Rather, we found that African-American race and traditional vascular risk factors, including older age, greater pack-years of smoking, and higher systolic blood pressure were associated with PAD. While HIV and HCV infection have been associated with a greater risk of CVD, they did not confer an association with PAD beyond that of traditional vascular risk factors in our study. Distinct patterns of risk factors have been reported across different vascular beds and cardiovascular subtypes. Future studies are needed to better understand how HIV and HCV infection impact different CVD subtypes in women.

The PAD prevalence observed in our cohort is of significant clinical concern given that general population studies have reported lower rates in similar aged adults. In the Framingham Offspring Study, a 3.6% prevalence of PAD (ABI<0.9) was observed in adults with a mean age of 59.[9] Another general population study found that African-Americans had a higher prevalence of PAD (ABI≤0.9) than Caucasians; African-American women had an age-adjusted prevalence of 4.4% prevalence compared to 3.2% in Caucasian women.[10] The mean age of women in that study was 53 years for African-Americans and 54 years for Caucasians. The prevalence of PAD reached 7.9% in African-American women ages 60-64 and 4.2% in Caucasian women ages 60-64. In our study, we also observed that African-American women had a greater risk of PAD compared to Caucasian women, but the prevalence of PAD in our overall cohort was substantially higher than that study. Another study in HIV-seronegative adults found that African-American women in the 50-59 year age range had a PAD prevalence of 3.4%, which rose to 8.9% in those 60-69 years, 20% in those 70-79 years, and 35% in those 80 or greater.[39] Taken together, our findings show that African-American women with and at risk for HIV and HCV infection in the U.S. may have a prevalence of PAD that is similar to African-American women in the general population who are 5-10 years older. These findings may be driven by the high prevalence of traditional CVD risk factors in our cohort.

Our findings suggest that HIV and HCV infections are not significant drivers of the high prevalence of PAD, which is in contrast to two of the largest studies of PAD that included PLWH and a comparison group of HIV seronegative patients. A possible explanation is that our cohort enrolled seronegative women based upon having similar HIV risk behaviors as women with HIV infection. Seronegative women in our cohort had a high prevalence of smoking, which is a risk factor for PAD. By contrast, in the study from Copenhagen, the

comparison group was from a general population study where the prevalence of smoking was significantly less than those with HIV infection.

Consistent with the findings from other studies, we found that traditional CVD risk factors are important factors associated with PAD. We specifically found that smoking and higher systolic blood pressure were strongly associated. Our finding that current statin use was associated with PAD, could be due to prescribing patterns of statin medications for patients with traditional vascular risk factors, cardiovascular disease, and higher ASCVD risk scores. Interestingly, the prevalence of smoking and hypertension in our cohort appeared greatest in the HCV-seropositive women. Although HCV therapies can now cure most persons with HCV infection, our findings suggest that these women may continue to be at significant risk for PAD even after HCV cure due to behavioral or other unmeasured factors. Interventions targeting smoking cessation and blood pressure control at earlier ages in women with and at risk for HIV and/or HCV infection may be important to decrease the risk of PAD and its sequelae. Among HIV-seropositive women, the lack of an association of CD4 count, HIV viral load, and HIV duration with greater odds of PAD could be because a large proportion of our women had a CD4 count above 500 and undetectable HIV viral load. Our findings provide support that traditional CVD risk factors (and not HIV-related immunosuppression) are associated with PAD.

Unexpectedly, we found that after adjustment for demographic, behavioral, and other CVD factors, the association of diabetes with PAD in our cohort was attenuated and no longer significant. Prior epidemiologic studies have found an association between diabetes and PAD, but diabetes may be associated with PAD progression in small rather than large vessels.[40-44] The ABI is a more sensitive measure of large vessel disease than small vessel disease. Our findings may also be explained by the relatively young age of our cohort and thus possibly shorter duration of diabetes leading to ABI values that either did not reach the cut off level for PAD or were spuriously high due to incomplete compression of vessels from diabetes-associated stiffening of the vasculature (i.e., ABI ≥ 0.9 but <1.4 which is the cutoff for non-compressible vessels). Studies using the toe-brachial index measurement, which captures small vessel disease and is less affected by stiff vessels, need investigation in our population.

Our findings represent the largest and most comprehensive study of PAD in women with and at risk for HIV infection and HCV infection. Nevertheless, there are limitations to our study. We employed a cross-sectional design; our participants were relatively young, but this also enabled us to identify a high PAD prevalence in middle-aged women with and at risk for HIV. The WIHS is a survivor cohort, so may not be generalizable to other women in the U.S. Additionally, some infection groups were smaller than others (for example, the HCV-monoinfection group had <100 women), so group-specific findings may need to be carefully interpreted. Participants with HIV had mostly well-controlled HIV, limiting our ability to examine the association of viremia with PAD. In addition, the interaction analysis should be interpreted with caution due to low prevalence of PAD and the relatively small sample size for some of the infection groups examined.

Conclusions

The high prevalence of PAD in our cohort of women is of clinical concern. Contrary to our hypothesis, HIV and HCV infections are not significantly associated with an increased risk of PAD. Our findings suggest that targeted interventions to reduce smoking and control blood pressure are critically important in women with and at risk for HIV, particularly African Americans. Longitudinal studies and examinations of the long-term sequelae of PAD, including physical function decline, are currently underway.

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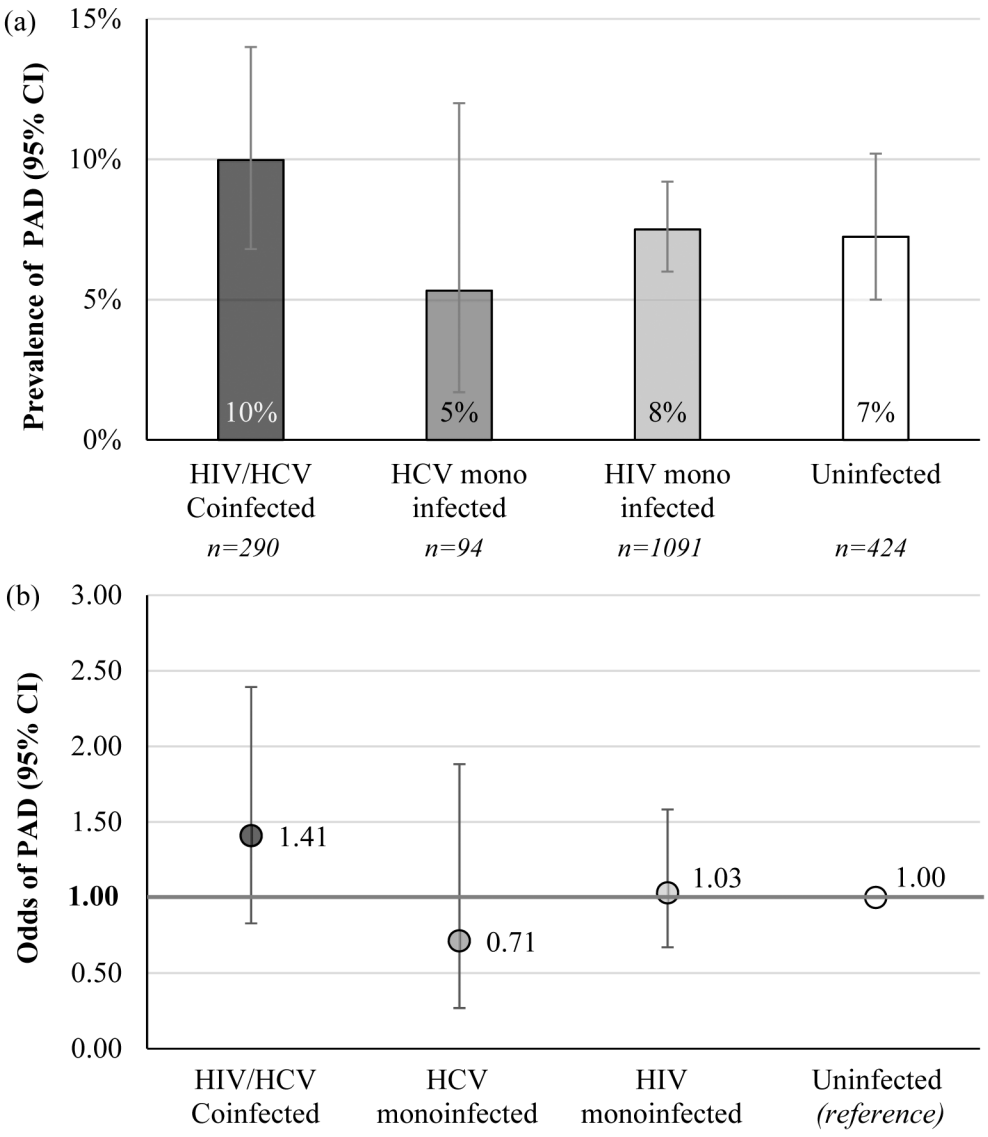

Figure 1:

(a) Prevalence of PAD by infection group. PAD defined by highest ankle pressure divided by highest arm pressure ≤0.9 and (b) Unadjusted odds of PAD in those with HIV/HCV coinfection, HCV monoinfection, and HIV monoinfection compared to uninfected controls. Footnote: The prevalence of PAD by infection status: HIV/HCV coinfection (n=29), HCV monoinfection (n=5), HIV monoinfection (n=82), neither HIV nor HCV infection (n=31)

Table 1:

Demographic and clinical characteristics of 1,899 WIHS women by HIV and HCV infection status.

Characteristics *Median (IQR) or %*	**HIV/HCV coinfected (n=290)**	**HCV-monoinfected (n=94)**	**HIV-monoinfected (n=1091)**	**Uninfected (n=424)**
Demographics				
Age (yrs)	55 (51, 58)	54 (48, 59)	49 (45, 54)	50 (45, 55)
Race				
African American	69% (199)	71% (67)	71% (774)	74% (314)
White	14% (42)	7% (7)	11% (119)	6% (27)
Other[¶]	2% (5)	6% (6)	4% (39)	5% (23)
Hispanic	15% (44)	15% (14)	15% (159)	14% (60)
Post-menopausal	79% (231)	70% (66)	51% (562)	49% (207)
Lifestyle				
Current smoker	56% (162)	73% (69)	35% (382)	46% (195)
Pack-years of smoking	10.6 (1.9, 18.5)	15.5 (8.2, 22.0)	0.7 (0, 9.6)	3.7 (0, 12.2)
Alcohol consumption				
None	59% (170)	53% (50)	56% (610)	41% (175)
Light (<15gm/day)	26% (75)	26% (24)	32% (354)	39% (162)
Moderate (15-30 gm/day)	6% (17)	5% (5)	4% (44)	8% (33)
Heavy (>30gm/day)	10% (28)	16% (15)	8% (82)	13% (54)
Metabolic				
BMI (kg/m^2)	27 (24, 32)	32 (26, 36)	30 (26, 36)	32 (27, 37)
Waist circumference (cm)	95 (85, 106)	102 (92, 112)	99 (89, 111)	103 (90, 112)
Hip circumference (cm)	101 (92, 110)	107 (98, 116)	106 (97, 115)	108 (100, 118)
Diabetes	23% (67)	33% (31)	21% (228)	24% (100)
HOMA-IR	2.97 (1.83, 5.22)	5.17 (2.02, 7.17)	2.54 (1.47, 4.21)	2.11 (1.17, 4.47)
Triglycerides (mg/dL)	111 (88, 155)	106 (74, 133)	103 (76, 146)	99 (71, 146)
HDL (mg/dL)	55 (42, 68)	51 (44, 66)	52 (43, 64)	55 (45, 67)
LDL (mg/dL)	84 (65, 107)	86 (68, 111)	103 (83, 125)	106 (83, 124)
Statin use				
Current	7% (19)	3% (3)	17% (182)	14% (59)

Characteristics *Median (IQR) or %*	HIV/HCV coinfected (n=290)	HCV-monoinfected (n=94)	HIV-monoinfected (n=1091)	Uninfected (n=424)
Ever	22% (64)	23% (22)	33% (356)	31% (133)
eGFR (ml/min/yr)	83 (65, 102)	94 (79, 108)	92 (77, 108)	97 (81, 109)
APRI	0.46 (0.28, 0.81)	0.40 (0.24, 0.63)	0.23 (0.16, 0.31)	0.19 (0.14, 0.25)
Hypertension	63% (183)	64% (60)	51% (553)	52% (222)
SBP (mmHg)	123 (112, 138)	126 (116, 144)	122 (111, 134)	123 (113, 139)
DBP (mmHg)	77 (72, 85)	78 (71, 84)	75 (69, 82)	77 (70, 83)
ASCVD score	5.65 (2.18, 10.1)	7.4 (2.5, 13.39)	2.7 (1.12, 6.54)	3.48 (1.12, 9.14)
HIV related				
CD4 T cell count (cells/mm^3)				
Current	590 (382, 787)	-	590 (392, 818)	-
Nadir	207 (100, 329)	-	221 (101, 351)	-
History of AIDS	40% (117)	-	31% (340)	-
Current ARV use	84% (243)		90% (978)	
Undetectable HIV RNA (≤20)	64% (184)	-	69% (754)	-

HCV, hepatitis C virus; IQR, interquartile range; BMI, body mass index; HOMA-IR, homeostasis model assessment of insulin resistance; HDL, high density lipoprotein; LDL, low density lipoprotein; eGFR, estimated glomerular filtration rate; APRI, AST platelet ratio index; ARV, antiretroviral drug

¶Includes Asian, Pacific Islander, Native American, Alaskan and other study participants

Table 2:

Association of HIV and HCV infection status with PAD.

Models*	HIV/HCV coinfected vs. uninfected OR (95% CI)	HCV monoinfected vs. uninfected OR (95% CI)	HIV monoinfected vs. uninfected OR (95% CI)
Demographic Adjusted	1.13 (0.66, 1.96) p=0.65	0.61 (0.23, 1.62) p=0.32	1.04 (0.67, 1.60) p=0.88
Demographic Adjusted + Behavioral	1.04 (0.60, 1.81) p=0.89	0.54 (0.20, 1.46) p=0.22	1.04 (0.67, 1.61) p=0.86
Demographic Adjusted + Behavioral + Vascular	1.09 (0.55, 2.15) p=0.80	0.53 (0.17, 1.65) p=0.28	0.98 (0.59, 1.65) p=0.94
Demographic Adjusted + Behavioral + Vascular + Liver	1.19 (0.57, 2.49) p=0.65	0.58 (0.19, 1.84) p=0.35	1.02 (0.61, 1.74) p=0.93

*demographic: age, sex, race; behavioral: smoking and alcohol; vascular: waist circumference, DM, HDL, LDL, GFR, pulse pressure (=systolic blood pressure – diastolic blood pressure); liver: AST-platelet ratio index (APRI)

Table 3:

Univariable and multivariable-adjusted associations of demographic, lifestyle, and vascular risk factors with presence of PAD in 1,899 participants.

Covariates	Univariable Odds Ratios (95% CI)	Multivariable Odds Ratios (95% CI)
HIV vs. uninfected	1.17 (0.79, 1.73)	1.32 (0.87, 1.99)
HCV vs. uninfected	1.21 (0.81, 1.80)	1.11 (0.70 1.76)
Age 51-60 vs. 40-50	**1.46 (1.01, 2.13)**	1.17 (0.70, 1.94)
61-70 vs. 40-50	**2.81 (1.71, 4.60)**	**2.01 (1.04, 3.87)**
African American	1.78 (0.92, 3.46)	**2.30 (1.15, 4.63)**
Menopause	0.81 (0.44, 1.49)	0.62 (0.32, 1.22)
Smoking (per 10 pack-yr)	**1.22 (1.07, 1.40)**	**1.27 (1.09, 1.48)**
Waist circumference (per 10cm)	**1.11 (1.01, 1.23)**	1.09 (0.97, 1.22)
Diabetes	**1.48 (1.02, 2.14)**	1.01 (0.66, 1.54)
Triglyceride (per 10 mg/dL)	**1.02 (1.00, 1.03)**	1.01 (0.99, 1.03)
LDL (per 10 mg/dL)	**1.06 (1.00, 1.12)**	1.05 (0.99, 1.11)
SBP (per 10 mm Hg)	**1.12 (1.04, 1.22)**	**1.14 (1.01, 1.28)**
DBP (per 10 mm Hg)	1.03 (0.88, 1.21)	0.83 (0.66, 1.05)
Current statin use	**2.09 (1.39, 3.13)**	**1.80 (1.15, 2.83)**