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Kaitlin Cirulli Date

Cardiovascular Risk Factors and Cardiac Biomarkers in Veterans Living with HIV and Uninfected Individuals

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Master of Public Health

Global Epidemiology

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Cardiovascular Risk Factors and Cardiac Biomarkers in Veterans Living with HIV and Uninfected Individuals

By

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Bachelor of Science

North Carolina State University

2016

Faculty Thesis Advisor: Alvaro Alonso, MD, PhD

An abstract of

A thesis submitted to the Faculty of the

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Abstract

Cardiovascular Risk Factors and Cardiac Biomarkers in Veterans Living with HIV and Uninfected Individuals

By Kaitlin Cirulli

Background: Non-communicable diseases have increased in people living with HIV; in particular, the risk of developing cardiovascular disease is two-fold higher in HIV-positive individuals.

Methods: Forty HIV-positive participants and uninfected individuals were recruited from the Atlanta VA Medical Center. Cardiovascular risk factors were collected through physical exams and paper questionnaires, and the following biomarkers were measured: high-sensitivity C-reactive protein (hsCRP), galectin-3, amino terminal propeptide of B-type natriuretic peptide (NT-proBNP), troponin T (TnT), and 3-nitrotyrosine (3-NT). Cardiovascular health was defined using the American Heart Association's Life's Simple 7. Multivariable logistic regression and multiple linear regression was conducted to evaluate the association of HIV infection status with risk factors and biomarkers of interest.

Results: HIV-positive participants on average scored 1.7 points higher (95% confidence interval: 0.9, 2.4) than uninfected individuals for the measure of overall cardiovascular health. HIV-positive participants were more likely to report a history of smoking and moderate exercise and less likely to report being a current smoker, use of medications for cholesterol, and use of medications for blood pressure. Additionally, HIV-positive participants had higher concentrations of hsCRP, galectin-3, and TnT values, and lower NT-proBNP and 3-NT values; however, these findings were not statistically significant.

Conclusions: In general, HIV-positive participants had better levels of cardiovascular health than uninfected individuals; however, biomarker results indicate a potentially greater risk for cardiovascular disease in the future.

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Table of Contents

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Kaitlin Cirulli

ABSTRACT

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INTRODUCTION

While the life expectancy and overall quality of life for people living with human immunodeficiency virus (HIV) continue to improve thanks to combination antiretroviral therapy (cART), a rise in comorbidities associated with non-communicable diseases such as liver, renal, and cardiovascular disease (CVD) is emerging in HIV-infected patients (1). The leading cause of mortality across the globe, cardiovascular disease, has not spared the HIV-positive population, as the global burden of CVD associated with HIV has tripled in recent years (2). A greater risk for developing cardiovascular disease has also developed for people living with HIV (2).

Traditional risk factors for CVD include high blood pressure, high cholesterol, diabetes, smoking, obesity, physical inactivity, family history of CVD, and older age (3). Additional indices for CVD risk include blood cardiac biomarkers. Specifically, several biomarkers can evaluate risk for primary cardiovascular events in populations without a history of CVD (4). These biomarkers can identify the vulnerability associated with an increased risk for CVD. For example, C-reactive protein (CRP), a biomarker of inflammation, has shown a strong association with cardiovascular disease risk in populations without a history of cardiovascular disease and is linked to arterial vulnerability (4, 5). Evidence also exists for biomarkers including nitrotyrosine, a marker of oxidative stress, and natriuretic peptides, markers of cardiac overload, to identify arterial vulnerability and to have a strong link to disease prospectively (5). Similarly,

troponin identifies myocardial vulnerability and has shown to have good evidence of a link to CVD prospectively (5). Few studies have investigated these biomarkers in individuals living with HIV.

This study aims to see which, if any, of these cardiac biomarkers differ according to HIV status. The biomarkers used in this study include the following: high-sensitivity C-reactive protein (hsCRP), galectin-3, amino terminal propeptide of B-type natriuretic peptide (NT-proBNP), troponin T (TnT), and 3-nitrotyrosine (3-NT). hsCRP has been associated with coronary artery disease and myocardial infarction (6). NT-proBNP has also been associated with myocardial infarction, as well as with heart failure and hypertension (6). Specifically, NT-proBNP has been indicative of heart failure in patients that are exhibiting CVD symptoms and of left ventricular dysfunction in asymptomatic subjects (7). Galectin-3 has been associated with cardiac fibrosis and incident heart failure (8). Lastly, TnT has been associated with cardiomyopathy, and 3-NT has been indicative of atherosclerosis (6, 9). This study aims to determine the association of HIV infection status with cardiovascular risk factors, markers of cardiovascular health, and the previously mentioned cardiac biomarkers.

METHODS

Study Population and Procedure

HIV-positive participants were selected from the HIV Atlanta Veterans Affairs Cohort Study (HAVACS), described in detail elsewhere (10). HAVACS was initiated in 1982 and is an extensive database of every HIV-positive patient ever seen at the Atlanta VA Medical Center (AVAMC). The uninfected participants in this study were veterans receiving primary care services at the AVAMC. Twenty uninfected participants were

matched one to one to the 20 HIV-positive participants by sex, race, and age (grouped as less than 50 and 50 or greater).

Individuals were screened for existing cardiovascular disease, and inclusion in this study required participants to be free of cardiovascular disease, such as coronary artery disease, substantial arrhythmias, valvular disease, heart failure, stroke, and pericarditis. Patient charts were also screened to exclude any participants with evidence of renal disease, determined by a serum creatinine greater than 1.5 mg/dL or eGFR less than 60 mL/min/1.73m^2. Lastly, any contraindications for MRI excluded potential participants.

Eligible participants were mailed an invitation letter describing the study and providing instructions to contact the research coordinator to proceed further or opt-out of the study. One hundred ten letters were mailed to potential HIV-positive participants and 100 letters were mailed to potential uninfected participants. Two weeks after these letters were mailed, participants were contacted by phone to identify potential interest and confirm eligibility requirements. Ninety-four HIV-positive individuals were contacted, and 79 uninfected individuals were contacted. Of those, 20 positive and 20 uninfected participants completed the enrollment process.

Participants first met with the research coordinator to obtain written informed consent and authorize the release of protected health information for research purposes. The participant then completed a paper questionnaire collecting medical history and diet and lifestyle information. Upon completion of the questionnaire, a physical exam was performed, including measures for blood pressure, height, and weight. Lastly, a certified phlebotomist drew a sample of blood to be later analyzed for cardiac biomarkers. Once

the blood draw was complete, each participant was compensated. The Institutional Review Board at Emory University approved this study.

Cardiovascular Risk Factor and Covariate Ascertainment

Data for cardiovascular risk factors of interest and other covariates were collected through a paper questionnaire completed by each participant during his or her clinic exam. The questionnaire was provided to the participant while the research coordinator remained in the exam room to answer any questions. Additionally, a physical exam was conducted to measure blood pressure, height, and weight. The research coordinator measured blood pressure three times using an electronic blood pressure monitor, while the patient remained seated. Each measurement was collected one minute apart. Standing height and weight were also measured by the research coordinator. Participant age and race was extracted from the patient's medical chart on the day of enrollment.

In order to obtain a measure of each participant's overall cardiovascular health, a composite measure was created based on the American Heart Association's (AHA) construct of ideal cardiovascular health, Life's Simple 7, consisting of seven health behaviors and health factors (11). For the purposes of this study, a similar composite variable was created, with one point for each metric that the participant meets, based on the AHA's ideal cardiovascular health definition and the available data. Ideal smoking status was met if the participant reported not having smoked any cigarette in the last 30 days. BMI was met if the calculated BMI was less than 25 kg/m^2. Sufficient physical activity required participants to report greater than or equal to 150 minutes per week of moderate exercise or 75 minutes per week of vigorous exercise. A healthy diet required reporting four of the following five standards: greater than or equal to four and a half

cups of fruits and vegetables per day, greater than or equal to two servings of fish per week, greater than or equal to three servings of whole grains per day, less than 1500 mg of sodium per day, and less than 36 ounces of sugar-sweetened beverages per week. Ideal cholesterol was considered met if the participant reported no history of hypercholesterolemia. Ideal blood pressure was met if the participant's average blood pressure was less than 120/80 mmHg. Lastly, fasting plasma glucose was considered met if the participant reported no history of diabetes. If the participant did not meet the criteria previously listed, they would earn zero points for that metric. The final range of this composite variable was from zero, indicating the worst cardiovascular health, to seven, indicating the best cardiovascular health.

Cardiac Biomarker Ascertainment

Cardiovascular biomarkers were measured from serum and plasma processed using standard procedures. These aliquots were stored at -80ºC and thawed immediately prior to performing each assay at the Rollins School of Public Health. Laboratory technicians were blinded to HIV status. High-sensitivity C-reactive protein (hsCRP), galectin-3, amino terminal propeptide of B-type natriuretic peptide (NT-proBNP), and troponin T (TnT) were measured on serum samples using the Meso scale platform and biomarker-specific antibody sets on streptavidin-coated plates. 3-nitrotyrosine (3-NT) was measured on plasma samples using the 3-nitrotyrosine enzyme-linked immunosorbent assay (ELISA) kit from Abcam (ab116691).

Statistical Analysis

Data analysis was performed using SAS, Version 9.4. In order to avoid confounding by certain known cardiovascular risk factors and to have an adequate distribution of demographics in both infected and uninfected participants, HIV-positive participants were frequency matched to HIV-uninfected individuals by age, sex, and race. HIV infection status was the primary independent variable. All analyses adjusted for age, sex, race. Race was dichotomized as white and non-white. Initial analysis steps included calculating average systolic and diastolic blood pressure values from the three individual measurements. Body mass index (BMI) was also calculated from measured height in centimeters and weight in kilograms. Additionally, all participants were confirmed eligible by examining questionnaire responses indicating a history of cardiovascular disease and confirming medications for exclusionary conditions were not being taken. Descriptive statistics were obtained for the study population overall and by HIV status.

Multivariable logistic regression was conducted to statistically evaluate the association of HIV infection status with the dichotomous outcomes, including the following cardiovascular risk factors: diabetes status, current smoking status, history of smoking, use of medications for high blood pressure, use of medications for high cholesterol, and moderate exercise. A current smoker was defined as someone who reported having smoked any cigarette in the last 30 days. History of smoking was defined as someone who had smoked more than 100 cigarettes in his or her lifetime. All models adjusted for age, sex, and race. One HIV-positive observation was removed from all analyses due to a missing value for race. By study design, all observations are considered independent. Cardiovascular risk factors chosen for analysis were assessed as

dichotomous categorical variables; participants selected either yes or no on the questionnaire provided during the clinic exam. Those who selected no were used as reference groups.

Multiple linear regression was conducted to statistically evaluate the association of HIV infection status with the continuous outcomes, including the cardiac biomarkers: hsCRP, galectin-3, NT-proBNP, TnT, and 3-NT. HIV infection status was the primary independent variable, and all models adjusted for age, sex, and race. Two HIV-positive observations were removed from all analyses due to a missing value for race and a hemolyzed lab sample leading to invalid biomarker results. Additionally, for analysis purposes, samples that reported undetectable TnT values were assigned a value of the limit of detection of 0.002 ng/mL divided by the square root of two, which equals .0014 ng/mL (12). As the distribution of means across participants did not appear normal for both hsCRP and NT-proBNP, the values were log-transformed and the linear regression analysis was repeated. Additionally, a non-parametric analysis was conducted for the NT-proBNP results using an exact Wilcoxon two-sample test. Multiple linear regression was also performed to analyze the association of HIV infectious status with the cardiovascular health composite variable, while controlling for age, sex, and race.

RESULTS

Results from the recruitment process are detailed in Figure 1 and did not appear to differ by HIV status. Few individuals reached out to study staff after receiving the introductory letter. A large number of individuals were never reached by telephone and did not respond to voicemails. Of those that were able to be reached, the most common reasons for ineligibility include moving out of the state and being ineligible for an MRI.

Additionally, several individuals who expressed interest and scheduled clinic appointments did not show or canceled their appointments and did not reschedule.

Selected characteristics of study participants are shown in Table 1 by total population and by HIV status. The average age at the time of exam was slightly higher for HIV-positive participants, but generally did not differ compared to that of the uninfected individuals. Both groups had equal distributions of males and females, with more males being enrolled. Additionally, the distribution of race among the two groups did not differ greatly. These results are expected, as we matched the uninfected participants to the positive participants by age, sex, and race. Several risk factors associated with CVD had fairly similar distributions among positive and uninfected individuals, including current smoking status and moderate exercise. The remaining risk factors, including BMI, blood pressure, and diabetes status, appear to have slight differences when comparing HIV-positive and uninfected participants as shown in Table 1. Notably, HIV-positive participants had better overall cardiovascular health, based on the composite cardiovascular health variable, at an average score of 4.4 compared to the uninfected individuals' score of 2.9.

As shown in Table 2, HIV-positive participants were more likely to report a history of smoking, when controlling for age, sex, and race; however, this finding was not statistically significant (OR = 1.42, 95% CI: 0.37, 5.44, p = 0.61). A similar association was found for moderate exercise. In contrast, HIV-positive participants were less likely to report being a current smoker, when controlling for age, sex, and race; however, this finding was also not statistically significant (OR = 0.74, 95% CI: 0.09, 6.05, p = 0.78). Reported use of medications for cholesterol showed a similar trend (OR = 0.45, 95% CI:

0.09, 2.15, p = 0.31). After controlling for age, sex, and race, HIV-positive status was statistically significantly associated with 20 times lower odds of reported use of medications for blood pressure (OR = 0.05, 95% CI: 0.01, 0.36, p = 0.004).

Cardiovascular biomarker results are shown in Table 3. One participant was removed from calculations due to a hemolyzed lab sample. Additionally, TnT was calculated using 19 samples that had detectable results. 12 of these samples were from HIV-positive participants and 7 were from uninfected individuals. The remaining 20 samples were assigned a value of 0.0014 ng/mL. HIV-positive individuals had higher levels of hsCRP, galectin-3, and TnT compared to uninfected individuals. For example, hsCRP, a biomarker of inflammation, was slightly above the total population average of 6.1 mg/L at 7.4 mg/L for HIV-positive participants, and lower than average for uninfected individuals at 4.9 mg/L. Contrastingly, HIV-positive participants had lower levels of both NT-proBNP and 3-nitrotyrosine compared to uninfected individuals.

Table 4 displays the multiple linear regression results for the association of HIV with cardiovascular health and biomarkers. On average, HIV-positive participants scored 1.7 points higher than uninfected individuals, and this result was statistically significant (95% CI: 0.9, 2.4, p < 0.0001). HIV-positive participants measured hsCRP values that were 2.9 mg/L greater on average than uninfected individuals; however, this association was not statistically significant (95% CI: -2.5, 8.3, p = 0.29). After log-transforming the hsCRP values and repeating the regression analysis, the results remained the same. Similar findings occurred for galectin-3 (2.6 ng/mL greater) and TnT (0.01 ng/mL greater). Contrastingly, HIV-positive participants measured 3-nitrotyrosine values that were 35.5 ng/mL lower than uninfected individuals on average; however, this finding was

not statistically significant (95% CI: -171.1, 100.1, p = 0.60). There was a similar trend with the NT-proBNP values (134.9 pg/mL lower), and this result was statistically significant (p = 0.032). However, after log-transforming the NT-proBNP values to address the failed assumption of normality, although an inverse association remains, the result is no longer statistically significant (p = 0.25). Lastly, the results of the exact Wilcoxon two-sided test using the original NT-proBNP values confirmed a non-significant association of HIV infection status with NT-proBNP (p = 0.19).

DISCUSSION

This study aimed to measure the association of HIV infection status with health behaviors and cardiovascular risk factors as well as with cardiac biomarkers. HIV-positive individuals reported a history of smoking and moderate exercise more often than uninfected individuals. Contrastingly, current smoking status, use of medications for cholesterol, and use of medications for blood pressure were reported less often among HIV-positive individuals. Additionally, higher levels of hsCRP, galectin-3, and TnT values were found in the HIV-positive population as well as lower levels of NT-proBNP and 3-nitrotyrosine. Overall, HIV-positive participants revealed a trend of better health and specifically, better cardiovascular health; however, biomarker results may indicate greater risk for cardiovascular disease in the future.

Previous studies have found higher proportions of hypertension, diabetes, and dyslipidemia in HIV-positive populations, and these particular factors have been associated with an increased risk of CVD (13, 14). The results of this study, however, led to opposite conclusions. HIV-positive individuals were less likely to report medication use for high cholesterol or blood pressure, and diabetes was non-existent in the HIV-

positive group. Similarly, previous studies analyzing the entire Veterans Aging Cohort Study (VACS) and the HAVACS subset found HIV-positive individuals to be less likely to have hypertension, diabetes, high cholesterol, and high BMI (15, 16). Additionally, smoking has been a commonly found risk factor in HIV-positive populations (17). While a history of smoking was more likely to be reported among HIV-positive participants in this study, current smoking was less likely to be reported. Lastly, overall levels of cardiovascular health were higher in HIV infected individuals than uninfected participants. HIV-positive participants seemed to produce outcomes indicating more beneficial overall health than uninfected individuals. As previously discussed, this trend was also found in studies analyzing the HIV-positive population at the Atlanta VA. This conclusion could be specific to the veteran population or this geographic location in particular. Additionally, people infected with HIV may seek care more frequently than uninfected individuals, leading to better overall health.

Biomarkers of inflammation, high-sensitivity C-reactive protein and galectin-3, have been associated with severity and prognosis of heart failure (18). Previous studies have found HIV-positive individuals to have significantly higher levels of both hsCRP and galectin-3 compared to uninfected individuals (19, 20). While this study supports these higher levels in infected individuals, the results were not significant. NT-proBNP, a marker of cardiac overload, has also been found to help diagnose and determine the prognosis of heart failure as well as other cardiovascular diseases such as atrial fibrillation and pulmonary hypertension (21). While several studies have found that levels of NT-proBNP are elevated in HIV-infected individuals (22), additional evidence exists that certain therapies have decreased NT-proBNP levels in people living with HIV (23,

24). The results of this study confirm the lower levels of NT-proBNP among individuals with HIV; however, further manipulation of the NT-proBNP values resulted in insignificant associations. Troponin T is a biomarker of myocardial vulnerability, and one previous study has shown elevated levels in a quarter of patients with acute HIV infection; however, these levels significantly declined after viremic control (25). In our study, higher levels of TnT were associated with HIV infection, but this result was not statistically significant. Since only 19 samples had detectable values, this result should be considered insufficient to draw a conclusion. Lastly, few studies exist analyzing 3-nitrotyrosine, a biomarker of oxidative stress and an indicator of atherosclerosis, in HIV-positive individuals. One study found that cells exposed to both the hepatitis C virus and HIV resulted in significantly increased production of 3-NT; however, exposure to HIV alone resulted in no significant effect (26). An additional study found elevated levels of 3-NT in rats that received exposure to cART (27). The results of our study are inconsistent with these previous findings, as lower levels of 3-NT were associated with HIV-positive individuals; however, this result was not statistically significant.

It is important to address several limitations in the study. The most notable limitation is the small sample size. This study was designed as a pilot study to gather initial research in order to help develop a larger proposal. Although there was a small number of participants, study staff were able to ensure that participants completed all aspects of the study, leading to a minor amount of missing data. Interviewer bias is an additional limitation in this study, as the study coordinator remained in the exam room as each participant completed the paper questionnaire requesting information about medical history as well as diet and lifestyle. Lastly, the study population consisted of 70% men.

Although this is expected when working with the veteran population, there would ideally be an equal representation of sex. Since the entire population consisted of veterans seeking care at the Atlanta VA, these results may not be able to be extrapolated to a non-veteran population or patient populations in other geographical areas.

Future research could further investigate how co-infections, such as tuberculosis or hepatitis in conjunction with HIV infection, affect the association of HIV infection with cardiovascular risk factors and health behaviors. Including comorbidities such as alcoholism or certain chronic diseases may also lead to additional conclusions. Additionally, incorporating time by following a cohort of HIV-positive individuals and looking for incident CVD may help researchers understand the true risk of CVD. Further analysis involving a comparison of drug therapies among HIV-positive individuals may provide insight into why these associations between infection status and cardiovascular health exist. In conclusion, this study provides validity to develop a much larger study in order to investigate true associations between HIV infection and cardiovascular disease. Our findings suggest that differences may occur in risk of developing CVD among HIV-positive individuals, supporting the conclusions of previous studies that appropriate risk modification strategies are important when determining the treatment for HIV-infected individuals.

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TABLES

Table 1. Demographic and Clinical Characteristics of Study Participants Overall and by HIV Status

Characteristic	Total Population[a] (n=40)	HIV Positive (n=20)	Uninfected Individuals (n=20)
Age at time of exam, years	49.4 (8.7)	50.4 (8.4)	48.4 (9.1)
Sex, N (%)			
Male	28 (70)	14 (70)	14 (70)
Female	12 (30)	6 (30)	6 (30)
Race, N (%)			
White	19 (48)	9 (45)	10 (50)
Non-white	20 (50)	10 (50)	10 (50)
Declined to answer	1 (2)	1 (5)	0 (0)
Body Mass Index, kg/m^2	31.1 (7.1)	30.9 (6.9)	31.4 (7.5)
Diabetes status, N (%)			
Yes	3 (8)	0 (0)	3 (15)
No	36 (90)	19 (95)	17 (85)
Unsure	1 (2)	1 (5)	0 (0)
Current smoker,[b] N (%)			
Yes	6 (15)	2 (10)	4 (20)
No	34 (85)	18 (90)	16 (80)
History of smoking,[c] N (%)			
Yes	15 (38)	8 (40)	7 (35)
No	25 (62)	12 (60)	13 (65)
Systolic blood pressure, mm Hg	122.3 (14.8)	115.1 (9.0)	129.6 (16.0)
Diastolic blood pressure, mm Hg	80.1 (10.7)	76.6 (8.6)	83.6 (11.6)
Use of medications for high blood pressure, N (%)			
Yes	17 (42)	4 (20)	13 (65)
No	23 (58)	16 (80)	7 (35)
Use of medications for high cholesterol, N (%)			
Yes	12 (3)	5 (25)	7 (35)
No	28 (70)	15 (75)	13 (65)
Moderate exercise, N (%)			
Yes	32 (80)	17 (85)	15 (75)
No	8 (20)	3 (15)	5 (25)
Assessment of overall health status, N (%)			
Excellent	6 (15)	4 (20)	2 (10)
Very good	16 (40)	8 (40)	8 (40)
Good	17 (43)	8 (40)	9 (45)
Fair	1 (2)	0 (0)	1 (5)
Poor	0 (0)	0 (0)	0 (0)
Cardiovascular health indicator[d]	3.6 (1.4)	4.4 (1.2)	2.9 (1.1)

Data given as mean (SD) unless otherwise specified.
[a]Individuals free of cardiovascular disease (coronary artery disease, substantial arrhythmias, valvular disease, heart failure, stroke, and pericarditis) were eligible.
[b]Current smoker defined as someone who has smoked any cigarette in the last 30 days.
[c]History of smoking defined as someone who has smoked more than 100 cigarettes in his/her lifetime.
[d]Cardiovascular health indicator, ranging from worst of 0 to best of 7, was calculated based on the American Heart Association's (AHA) construct of ideal cardiovascular health consisting of the following 7 health behaviors and health factors: current smoking status, BMI, physical activity, diet, history of high cholesterol, blood pressure, and diabetes status (11).

Table 2. Estimated Odds Ratios (OR) and 95% Confidence Intervals (CI) for the Association of HIV with Cardiovascular Risk Factors in Study Participants, Controlling for Age, Sex, and Race

Characteristic	HIV Positive[a] (n=19)	Uninfected Individuals (n=20)	OR	95% CI		P-Value
Diabetes status						
No[b]	18	17				
Yes	0	3	NA	NA	NA	NA
Current smoker[c]						
No[b]	17	16	1.00			
Yes	2	4	0.74	0.09	6.05	0.78
History of smoking[d]						
No[b]	11	13	1.00			
Yes	8	7	1.42	0.37	5.44	0.61
Use of medications for high blood pressure						
No[b]	15	7	1.00			
Yes	4	13	0.05	0.01	0.36	0.004
Use of medications for high cholesterol						
No[b]	14	13	1.00			
Yes	5	7	0.45	0.09	2.15	0.31
Moderate exercise						
No[b]	3	5	1.00			
Yes	16	15	1.85	0.36	9.34	0.46

[a]One participant was removed from analysis due to missing race value.
[b]Reference group
[c]Current smoker defined as someone who has smoked any cigarette in the last 30 days.
[d]History of smoking defined as someone who has smoked more than 100 cigarettes in his/her lifetime.

Table 3. Cardiovascular Biomarker Results for Study Participants Overall and by HIV Status

Biomarker	Total Population[a] (n=39)	HIV Positive (n=19)	Uninfected Individuals (n=20)
High-sensitivity C-reactive Protein (mg/L)	6.1 (9.0)	7.4 (11.2)	4.9 (6.5)
Galectin-3 (ng/mL)	17.7 (8.8)	19.3 (9.4)	16.0 (8.1)
Amino Terminal Propeptide of B-type Natriuretic Peptide (pg/mL)	198.0 (186.5)	137.9 (70.1)	255.0 (240.6)
Troponin T (ng/mL)[b]	0.019 (0.02)	0.025 (0.03)	0.013 (0.02)
3-Nitrotyrosine (ng/mL)	1,088.4 (192.5)	1,069.5 (207.6)	1,106.4 (180.6)

Data given as mean (SD).
[a]One participant was removed due to a hemolyzed sample.
[b]TnT was calculated using 19 samples with detectable values. 12 were HIV-positive and 7 were uninfected individuals. The remaining 20 samples were assigned 0.0014 ng/mL.

Table 4. Multiple Linear Regression Results for the Association of HIV with Cardiovascular Health and Cardiovascular Biomarkers in Study Participants, Controlling for Age, Sex, and Race

	Estimate	95% Confidence Interval		P-Value
Cardiovascular health (score, range 0-7)[a]	1.7	0.9	2.4	<0.0001
Biomarker[b]				
High-sensitivity C-reactive Protein (mg/L)	2.9	-2.5	8.3	0.29
Log-transformed High-sensitivity C-reactive Protein (mg/L)	0.2	-0.8	1.2	0.75
Galectin-3 (ng/mL)	2.6	-2.5	7.7	0.31
Amino Terminal Propeptide of B-type Natriuretic Peptide (pg/mL)	-134.9	-257.5	-12.3	0.032
Log-transformed Amino Terminal Propeptide of B-type Natriuretic Peptide (pg/mL)	-0.4	-1.1	0.3	0.25
Troponin T (ng/mL)[c]	0.01	-0.01	0.03	0.19
3-Nitrotyrosine (ng/mL)	-35.5	-171.1	100.1	0.60

[a]Cardiovascular health indicator, ranging from worst of 0 to best of 7, was calculated based on the American Heart Association's (AHA) construct of ideal cardiovascular health consisting of the following 7 health behaviors and health factors: current smoking status, BMI, physical activity, diet, history of high cholesterol, blood pressure, and diabetes status (11).
[b]One participant was removed due to a hemolyzed sample.
[c]TnT was calculated using 19 samples with detectable values. 12 were HIV-positive and 7 were uninfected individuals. The remaining 20 samples were assigned 0.0014 ng/mL.

FIGURES

Figure 1. Recruitment Process Results for Eligible Participants