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Left Atrial Mechanics and Diastolic Function Amongst People with HIV: Insights from the Veterans Aging Cohort Study

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Abstract

HIV infection is associated with subclinical cardiomyopathy, diastolic dysfunction, and increased risk of cardiovascular death. However, the relationship between left atrial (LA) mechanics and left ventricular (LV) diastolic function has not been evaluated in people with HIV (PWH) relative to HIV-uninfected (HIV-) controls. A multi-center, cross-sectional cohort analysis using the HIV

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Cardiovascular Disease (CVD) sub-study of the Veterans Aging Cohort Study (VACS) database to examine a cohort of PWH and HIV- veterans without known CVD.A total of 277 individuals (180 PWH, 97 HIV-) with echocardiograms were identified. LV and LA phasic strain were derived and diastolic function was evaluated. Relationships between LA strain, LV strain, and the degree of diastolic dysfunction were assessed using ANOVA and ordinal logistic regression with propensity weighting. In the PWH cohort, 91.7% were on anti-retroviral therapy and 86.1% had HIV viral loads <500 copies/mL. The mean (±SD) duration of infection was 9.7±4.9 years. Relative to HIV- veterans, PWH did not differ in LA mechanics and proportion of diastolic dysfunction (p=0.31). Using logistic regression with propensity weighting, we found no association between HIV status and degree of diastolic dysfunction. In both cohorts, LA reservoir strain and LA conduit strain were inversely and independently associated with the degree of diastolic dysfunction. Compared with HIV- veterans, primarily virally-suppressed and antiretroviral-treated PWH did not differ in LA strain or LV diastolic dysfunction. If confirmed in other cohorts, HIV viral suppression may curtail adverse alterations in cardiac structure and function.

Keywords

Left atrial function; HIV; diastolic function; speckle-tracking strain; echocardiography

Introduction

HIV infection is considered by some to be equivalent to traditional cardiovascular risk factors such as hypertension, smoking, dyslipidemia, and diabetes mellitus.[1] People living with HIV (PWH) are at higher risk of coronary artery disease (CAD), stroke, and heart failure compared to individuals without HIV.[2] While viral suppression has been shown to decrease the risk of heart failure and sudden cardiac death,[3,4] PWH with viral suppression still have increased risk of heart failure compared to uninfected individuals.[5] While the factors and mechanisms responsible for the latter observation remain unclear, it is suspected that HIV infection causes alterations in cardiac function and structure that increase the risk of myocardial dysfunction, even in the setting of preserved left ventricular ejection fraction.[6,7]

The left atrium (LA) modulates left ventricular (LV) preload throughout the atrial cardiac cycle. During the LA reservoir phase, which occurs during ventricular systole, the LA expands as it passively fills against a closed mitral valve. During the conduit phase, the LA passively empties with the opening of the mitral valve in early ventricular diastole. In the contractile phase, which corresponds to late ventricular diastole, the LA contracts and ejects the remaining volume into the LV. Studying the interplay between LA structure and function and LV diastolic performance is essential to understanding diastolic dysfunction. Microstructural remodeling in either chamber modifies the overall work needed to maintain efficient performance, and alterations in LA mechanics may potentially precede that of other established markers of LV diastolic dysfunction.[8] For example, atrial enlargement or ventricular dilation may lead to altered LA phasic strain and LV strain measurements throughout the cardiac cycle.[9] As a diagnostic marker, LA reservoir strain has been shown to decrease with worsening diastolic dysfunction and to be independently associated with

cardiovascular mortality.[10,11] For applications related to diastolic function, evaluation of LV filling pressures, etiology of dyspnea, or prediction of cardiovascular events, LA phasic strain measurements were superior to traditional echocardiographic parameters and in some cases, the incorporation of LA phasic strain incrementally increased the performance of other parameters.[8,9,12] Although LV strain is increasingly important in the management and evaluation of heart failure,[13] LA mechanics remain under-characterized.

We hypothesized that even within a group of primarily virally suppressed PWH, the presence of HIV infection would cause a detectable difference in LA structure and function, namely by measurement of left atrial strain parameters and diastolic function analysis, compared to HIV- controls.

Materials and methods

The Veterans Aging Cohort Study (VACS) consists of veterans living with HIV matched 2:1 by age, sex, race/ethnicity to uninfected veterans across multiple clinical sites within the Veterans Affairs Healthcare System and has been previously described.[14] The VACS Cardiovascular Disease (VAC-CVD) substudy included subjects from three participating VACS sites (VA Pittsburgh, VA Baltimore, and VA Greater Los Angeles Healthcare Systems) with the goal of examining the association between HIV and cardiovascular disease. The Institutional Review Board at each clinical site approved the study and all enrolled participants gave written informed consent.

All participants enrolled in the VACS Cardiovascular Disease (VACS-CVD) substudy were eligible for inclusion if they had a normal left ventricular ejection fraction (LVEF >50%) by 2D-transthoracic echo (TTE). Participants were excluded if they had a history of myocardial infarction, known CAD, stroke or transient ischemic attack, a history of atrial fibrillation, or congestive heart failure at the time of enrollment.[3] PWH were considered to have virally-suppressed HIV if the plasma viral load was below 500 copies/mL. Participant demographics, medications, medical co-morbidities, and routine echocardiographic parameters reported in the VACS-CVD substudy were extracted from the VACS database.

All 2D-TTE images provided by the VACS-CVD substudy core were in DICOM format and were acquired with commercially available ultrasound systems (GE Medical or Phillips). The comprehensive echocardiographic examination performed in the VACS-CVD substudy was in accordance with the American Society of Echocardiography guidelines.[15]

We calculated the LV mass using the standard cube formula $(0.8 \times 1.04(\text{LVEDd} + \text{PWDd} + \text{IVSDd})^3 - \text{LVEDd}^3) + 0.6\text{g})$[16], where LVEDd is the end diastolic LV internal diameter, PWDd is the end diastolic posterior wall thickness, IVSDd is the end diastolic interventricular septal thickness. The parameters used in the computation of cardiac mass were obtained by the core lab. For the purpose of this analysis, diastolic dysfunction was assessed based on the following criteria: 1) Left atrial volume index (LAVI) >34 mL/m^2, 2) average E/e' ratio >14, 3) annular medial e' velocity <7 cm/s -OR- annular lateral e' velocity <10 cm/s, or 4) peak tricuspid regurgitant velocity >2.8 m/s.[17,18] The degree of diastolic

dysfunction for each patient was graded along the ordinal score of 0, 1, and ≥2 markers of diastolic dysfunction.

The image quality and frame rate were assessed for appropriateness of strain analysis. If image quality or frame rate were insufficient, the study was excluded from strain analysis. The reader performing the strain analysis was blinded from all other information. All strain parameters were derived from the standard apical long axis (4-chamber [A4C], 3-chamber [A3C], and 2-chamber [A2C]) and parasternal LV short axis (basal, mid, apical) views (2D Cardiac Performance Analysis v4.6, TomTec Imaging Systems). LV GLS (global longitudinal strain) values reflected an average measure of global strain values from the apical long axis images. LV GCS (global circumferential strain) values reflected the average circumferential strain from the basal, mid, and apical SAX images. LV GRS (global radial strain) values reflected the GRS values from SAX views and apical long axis views.

We derived LA strain values at each phase of the atrial cycle using the A4C view. The point of zero strain, also known as the reference point, was set at the R-wave. An example A4C image with endocardial tracing with corresponding LA strain curves is shown in Figure 1.

Continuous variables are reported as the mean ± standard deviation. Relationships between categorical variables were assessed using a Chi-squared test. We used a two-sided t-test to perform group comparisons of continuous variables. Where appropriate, ANOVA was used to perform comparisons between more than 2 groups of continuous variables. When ANOVA was used to evaluate diastolic dysfunction and strain parameters, linear trend estimation was utilized if results were $p < 0.10$. To assess the relationship between the degree of diastolic dysfunction and LA strain parameters, ordinal logistic regression analysis was used. The effect of HIV was selectively considered as a primary exposure by using propensity weighting that accounted for age, body mass index (BMI), and diagnoses of diabetes or hypertension. The effect of BMI on diastolic function was reported as per 5 kg/m^2 change and LA strain parameters were reported per 5% for strain and per 20%/sec for strain rate. Statistical significance was defined as a 2-sided P-value of <0.05. The Bonferroni correction was used to account for multiple comparisons where specified. All analyses were performed with SAS 9.4 (SAS Institute Inc., Cary, North Carolina, USA).

Results

A total of 304 participants with TTEs were identified, including 196 PWH and 109 HIV-uninfected Veterans. Twenty-two participants were excluded from further analysis due to corrupted data files, missing TTE data, or inadequate image quality. Five participants were excluded due to a history of atrial fibrillation. The final 277 participants included in this analysis consisted of 180 PWH and 97 HIV- individuals. Baseline characteristics and demographics for the PWH and HIV- groups are shown in Table 1. The subject-reported duration of HIV infection amongst the PWH cohort was 9.7±4.9 years (N=54). The HIV- cohort had a higher mean BMI and a higher proportion of obese individuals than the PWH cohort. While the number of participants with hypertension and the systolic blood pressure were not appreciably different by HIV status, the HIV- cohort used a higher number of blood pressure medications. There was also a higher prevalence of chronic obstructive pulmonary

disease in the HIV-uninfected group. There was a high prevalence of prior Hepatitis C (HCV) infection (either by laboratory serology confirmation or ICD-9 coding) in both cohorts.

Among the PWH cohort, 91.7% reported being on ART, 86.1% had HIV viral loads <500 copies/mL, median CD4 count was 459 cells/mm^3 (IQR [306, 666]) and median CD4 count nadir was 207 cells/mm^3 (IQR [99, 312] (Table 1).

Table 2 summarizes the relevant standard echocardiographic parameters for both PWH and the HIV- cohorts. HIV- participants had higher LV wall thickness and higher LV mass than the PWH; when corrected for BSA, the LV mass index was similar in both cohorts. There was no significant difference in LV internal diameter and volume between HIV- participants and PWH. The mean mitral inflow E/A ratios were not statistically different based on HIV status. While both medial and lateral tissue doppler velocities were similar by HIV status, there was a higher percentage of HIV- participants with reduced lateral e' (<10 cm/s). While the average E/e' ratios, which reflect LA pressure, were higher in the HIV- cohort (p=0.007), the average E/e' ratios from neither group met the cutoff of >14 to suggest increased LV filling pressure. We also did not detect a significant difference in LA volume based on HIV status.

We did not detect any differences in LV GLS, LV GCS, or LV GRS between PWH and HIV- groups, nor was a difference detected in the LA strain and strain rates during each of the atrial phases.

Most individuals (81.9%) had at least 1 marker of diastolic dysfunction. Reduced mitral annular tissue doppler velocity was the most common marker of diastolic dysfunction, occurring in 67% (N=187) of study individuals. Overall, there were no differences in the proportion with diastolic dysfunction between the PWH and HIV- cohorts (p=0.31), including in the number of individuals with ≥ 2 markers of diastolic dysfunction (23.7% vs 23.9%, for the HIV- group and PWH cohorts, respectively). In the PWH cohort, there was no significant difference in estimated duration of infection by degree of diastolic dysfunction.

The relationship between LA and LV strain parameters based on markers of diastolic dysfunction and HIV status is shown in Table S1 and graphically represented in Figure 2. LV strain parameters (GLS, GCS, GRS) were not significantly associated with the degree of diastolic dysfunction. In comparison, LA reservoir and conduit strains (and corresponding strain rates) not only showed a difference in values stratified by degree of diastolic dysfunction, but also fulfilled the test for linearity, suggesting that increased diastolic dysfunction was associated with impaired LA function. The relationship between strain parameters and diastolic dysfunction appeared to be similar in HIV- and PWH groups.

Results from multivariate logistic regression analysis was used to further evaluate the effect of HIV status on LA strain parameters (Table 3). Age and hypertension were associated with risk of diastolic dysfunction, while BMI, diabetes, history of prior hepatitis C infection, and HIV status were not. Propensity weighting was used to account for baseline differences between PWH and HIV- cohorts and to focus on the effect of HIV status on diastolic

dysfunction. After adjustment of our regression using propensity weighting, we still did not detect a statistically significant.

In our multivariate regression model with LA strain parameters, both reservoir strain and conduit strain were associated with increased risk of diastolic dysfunction, while contractile strain and strain rate were not (Table 3). Lower magnitude strain rates for each of the atrial phases were associated with increased degree of diastolic dysfunction. Of the three phases of the LA cycle, conduit phase strain and strain rate had the highest odds-ratio point estimate.

Discussion

This study evaluated differences in diastolic function of PWH relative to HIV-uninfected using speckle tracking derived LA strain and explored relationships between conventional measures of diastolic function and cardiac phase-resolved LA function. In this population of virally suppressed PWH with good viral control without systolic dysfunction (LVEF ≥50%), we did not identify an effect of HIV status on conventional echocardiographic doppler-derived measures of diastolic dysfunction or LA strain parameters. Our data support an inverse relationship between LA reservoir and conduit strain with diastolic function, which was not seen with contractile strain. These relationships were similar between a cohort of PWH who were mostly virally suppressed and a cohort of HIV-uninfected individuals with traditional cardiovascular risk factors.

While other studies have reported on LA mechanics in PWH, to our knowledge, this work is unique in its comparison LA strain parameters in PWH relative to that of HIV uninfected controls. The Characterization of Heart Function on Antiretroviral Therapy (CHART) study showed decreased LA reservoir strain and conduit strain in treated and virally suppressed PWH who had diastolic dysfunction while contractile strain was unchanged[7], a finding that has been replicated in other non-HIV populations.[10,18] We observed a similar inverse relationship between LA strain and diastolic dysfunction in virally suppressed PWH relative HIV- controls. Additionally, there were no significant differences between conventional echocardiographic derived markers of diastolic dysfunction.

While the E/e’ ratios in our cohort of uninfected control were higher than those belonging to PWH, the E/e’ ratio in both cohorts did not exceed the threshold that is typically used to infer increased LV filling pressure (E/e’>14). The HIV- cohort had higher mitral inflow E and lower lateral e’ velocities. At the core of diastolic dysfunction is the heart’s inability to relax. Echocardiographic parameters such as the pulse wave mitral annular tissue Doppler e’ velocity or the ratio of the E/e’ have been used to make inferences about LV relaxation. The mitral inflow early diastolic velocity E is affected by the LA-LV pressure gradient. E and e’ are related through a time constant of LV relaxation (tau, τ). Both mitral E and e’ are also affected by loading conditions and technical parameters at time of the Doppler signal acquisition. An inverse relationship between e’ and afterload exists such that high afterload is associated with lower e’ velocities. The e’ is also affected by LV elastic coil, i.e. the smaller the LV end-systolic volume the faster the elastic recoil and the higher the e’. In contrast, conditions such as mitral annular calcification can result in a reduced lateral e’ velocity and confound the use of e’ to assess diastolic function. In our current

analysis, comorbid conditions in the HIV- cohort might have contribute to the lower lateral e' velocities. Despite correcting for differences in cardiovascular risk factors with propensity weighting we did not find HIV as an independent risk factor for diastolic dysfunction.

Cardiac MRI studies have examined the effects of HIV infection in virally suppressed PWH. Compared to uninfected controls, HIV infection is associated with increased intramyocardial lipids and diffuse myocardial fibrosis, as well as evidence of myocardial inflammation, with more late gadolinium enhancement, prolonged T1 relaxation, and high T2 values.[19] LV thickness and mass were also increased[20] and LV mechanics were also altered, with decreased peak systolic and diastolic longitudinal strain.[21] In contrast, published echocardiographic data in the HIV population remain conflicting and may be attributable to differences in the derivation methods and vendor-specific software used for strain analysis. In a study comparing a highly comorbid PWH cohort with a wide range of viral control to healthy HIV- individuals, PWH had higher LV mass index, LAVI, and pulmonary artery systolic pressure by echocardiography. The same study also reported that HIV infection was independently associated with diastolic dysfunction after adjusting for age and presence of hypertension.[6] In another study, asymptomatic PWH had decreased LV GLS as well as strain rates during systole and early diastole compared to uninfected controls.[22]

The assumption in HIV-associated cardiovascular pathology is that myocardial fibrosis and inflammation, even in virally suppressed PWH, would contribute to subclinical systolic and diastolic dysfunction that would manifest as differences in LA mechanics. LA function is known to be an early marker of diastolic dysfunction, and alterations in function may occur prior to well established markers of dysfunction, including LA volume index or other non-invasive surrogates of LA pressure.[8] However, our results suggest no independent effects of HIV status on LA mechanics and markers of diastolic dysfunction, and therefore the magnitude of effect due to HIV is small in comparison to that of other traditional risk factors for diastolic dysfunction.

A major limitation of our study is the control cohort. Veteran subjects have been known to have higher likelihood of cardiovascular comorbidities.[23,24] Our HIV- veteran cohort had higher average BMI but insignificantly higher prevalence of hypertension, diabetes, alcohol use disorder, smoking, and COPD relative to the PWH group. From the standpoint of diastolic function, our negative finding bodes well for PWH with virally suppressed titers. Second, relative to the published 'normal' reference range for LV GLS (-15.9% to -22.1%), the lower average LV GLS seen in both PWH (−15.0% ± 3.0%) and uninfected controls (−15.6% ± 2.6%) suggests minimally impaired cardiac function.[25] It should be noted that both cohorts in our study are older and have higher prevalence of cardiovascular risk factors than the population from which the reference LV GLS range were ascertained. Third, the LA strain analysis in our current study was cross-sectional and does not capture the full spectrum of disease trajectory. Strain analyses were performed retrospectively and the echocardiographic images were primarily optimized for LV rather than LA evaluation. However, all echocardiographic images were inspected for quality and frame rate prior to inclusion into this analysis. Finally, approximately 50% of individuals in both the PWH and HIV- cohorts had a history of prior HCV infection, either by serology or medical coding. While not considered a traditional cardiovascular risk factor, HCV has been associated with

a variety of cardiomyopathies.[26] We were unable to identify a relationship between diastolic dysfunction and HCV by inclusion of HCV in the multi-variate logistic regression model, but we did not further examine interactions between HCV and HIV due to small sample sizes. The specific data of regarding HCV viral load, time of infection, and history of treatment were also not available for analysis.

In summary, LA strain by speckle-tracking echocardiography and markers of diastolic dysfunction did not differ between a cohort of primarily virally suppressed PWH and a HIV- control cohort with traditional cardiovascular risk factors. We were unable to identify any changes to LA structure or function or differences in diastolic function attributable to HIV infection. While virally suppressed PWH has been reported to have an increased risk of heart failure compared to uninfected controls, the increased risk likely represents a clinically insignificant effect size compared to that of traditional, and modifiable, cardiovascular risk factors.[5] Future investigations may consider longitudinal analysis of myocardial deformation and other mechanisms that may contribute to subclinical cardiomyopathy. As has been postulated previously, the primary method of reducing the risk of HIV-associated cardiomyopathy, both overt and subclinical disease, is adherence to ART and successful viral suppression.[1] Amongst the virally suppressed individuals, further risk reduction of cardiovascular disease may best be accomplished with mitigation and optimization of other traditional risk factors such as diabetes, hypertension, hyperlipidemia, obesity, and smoking.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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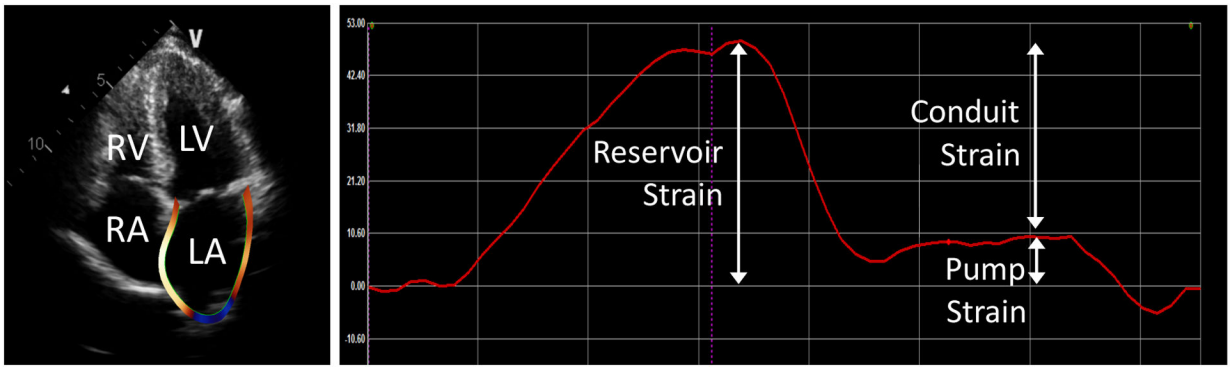

Figure 1.

Representative 2D transthoracic echocardiogram and illustrative left atrial strain curve. The *left panel* is a transthoracic echocardiographic image in the apical 4-chamber view at ventricular end-systole. The left atrium (LA) is segmented for strain analysis. The *right panel* is a typical LA strain curve for one cardiac cycle. Reservoir strain is the strain value at LV end systole. Contractile strain is the change in strain between left atrial contraction at late LV diastole and the beginning of LV systole. Reference point is set to the end of LV diastole (R-R gating). LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.

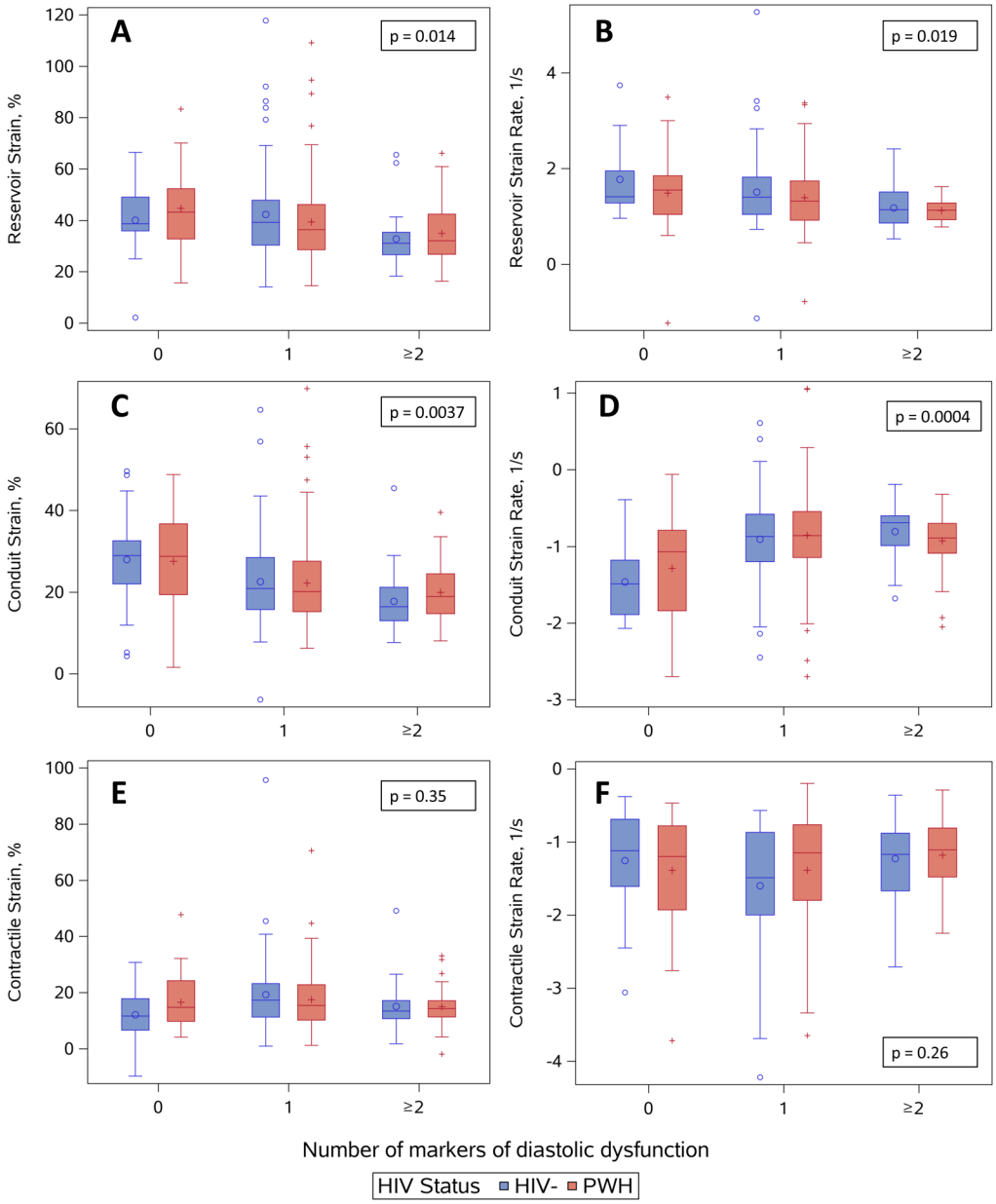

Figure 2:

Comparison of left atrial (LA) strain and markers of diastolic dysfunction in HIV- and people living with HIV (PWH). Relationship between number of markers of diastolic dysfunction and LA reservoir strain (A) and strain rate (B), LA conduit strain (C) and strain rate (D), LA contractile strain (E) and strain rate (F). Strain and strain rate are stratified by HIV status (HIV- = red, PWH = blue). The upper and lower edges of the box plot reflect the 75th and 25th percentiles and the midline reflects the median. The whiskers of the box plot represent the maximum value below the upper limit and minimum value above the lower limit, respectively. The upper limit is defined as 1.5(IQR) above the 75th percentile. The lower limit is defined as 1.5(IQR) below the 25th percentile. Outliers that are greater than

± 1.5(IQR) are indicated by markers. P values represent two-sided ANOVA for the PWH cohort. IQR, inter-quartile range

Table 1.

Demographics and characteristics of HIV-uninfected and PWH cohorts

	HIV neg (N=97)	PWH (N=180)	P value
Age, years	55.4 ± 6.8	54.0 ± 7.4	0.11
Male, N (%)	96 (99.0)	179 (99.4)	0.65
Race			0.91
White, % (N)	13 (13.4)	29 (16.1)	
Black, % (N)	77 (79.4)	136 (75.6)	
Hispanic, % (N)	5 (5.2)	11(6.1)	
Other, % (N)	2 (2.1)	4 (2.2)	
BMI, kg/m^2	28.7 ± 5.4	26.2 ± 4.6	<0.0001
>30, N (%)	34 (35.1)	30 (16.6)	0.0005
Diabetes Mellitus, N (%)	21 (21.7)	36 (20.0)	0.75
Hepatitis C, N (%) *	46 (47.4)	96 (53.3)	0.35
Hypertension, N (%)	64 (66.0)	110 (61.1)	0.42
Number of medications	1.6 ± 1.6	1.2 ± 1.3	0.019
Active tobacco use, N (%)	53 (54.6)	91 (50.6)	0.74
Statin therapy, N (%)	28 (28.9)	69 (38.1)	0.12
Total cholesterol, mg/dl	175.0 ± 35.7	174.2 ± 34.2	0.85
HDL, mg/dL	46.4 ± 16.9	43.5 ± 14.9	0.14
LDL, mg/dL	100.3 ± 30.4	98.1 ± 28.7	0.55
Triglycerides, mg/dL	156 ± 220	171 ± 152	0.48
NT-pro-BNP, pg/ml, median [IQR]	34 [15, 77]	36 [18, 87]	0.24
CD4 count, cells/mm^3, median [IQR]	--	459 [306, 666]	--
<200, N (%)	--	19 (10.6)	--
CD4 count nadir, cells/mm^3, median [IQR]	--	207 [99, 312]	
HIV viral load, copies/mL, median [IQR]	--	48 [40, 66]	--
<500, N (%)	--	155 (86.1)	--
Antiretroviral Therapy, % (N)	--	165 (91.7)	--

* History of hepatitis C, by laboratory analysis or ICD coding.

BMI, body mass index; BNP, brain natriuretic peptide; HDL, high-density lipoprotein; IQR, inter-quartile range; LDL, low-density lipoprotein

Table 2:

Echocardiographic parameters of HIV- control and PWH

Echo Parameters	HIV neg (N=97)	PWH (N=180)	P value[a]
LV internal diameter, diastolic, cm	4.70 ± 0.40	4.70 ± 0.48	1.00
LV internal diameter, systolic, cm	3.05 ± 0.40	3.05 ± 0.52	0.94
LV posterior wall, diastolic, cm	1.09 ± 0.15	1.02 ± 0.15	0.0005
Interventricular septal thickness, diastolic, cm	1.10 ± 0.17	1.04 ± 0.14	0.0019
LV end diastolic volume, mL	114.5 ± 34.7	111.7 ± 29.4	0.47
LV end systolic volume, mL	61.3 ± 22.7	59.8 ± 18.9	0.55
LV Mass (g)	188.6 ± 47.7	172.7 ± 41.8	0.0049
LV Mass index (g/m^2)	97.6 ± 22.3	93.2 ± 21.3	0.20
Mitral inflow E velocity, cm/s	65.3 ± 17.8	63.1 ± 14.8	0.28
Mitral inflow A velocity, cm/s	63.4 ± 15.1	60.5 ± 14.1	0.12
Mitral inflow E/A ratio	1.08 ± 0.38	1.09 ± 0.36	0.75
Markers of Diastolic Dysfunction			
e' (medial) velocity, cm/s	6.9 ± 1.9	7.3 ± 1.8	0.11
N% with <7 cm/s (N)	52.6 (51)	46.7 (84)	0.35
e' (lateral) velocity, cm/s	8.9 ± 2.5	9.6 ± 2.6	0.045
% <10 cm/s (N)	69.1 (67)	53.9 (97)	0.014
Average E/e' ratio	9.75 ± 3.05	8.97 ± 2.40	0.007
% >14 (N)	9.3 (9)	2.8 (5)	0.019
Peak tricuspid regurgitation velocity, cm/s	238.6 ± 29.5	236.8 ± 29.6	0.72
% >280 cm/s (N)	4.1 (4)	5.0 (9)	0.74
LA volume index, mL/m^2	27.5 ± 11.8	30.3 ± 12.2	0.059
% >34 mL/m^2 (N)	22.0 (24)	33.9 (61)	0.12
Deceleration Time, ms	211.9 ± 46.4	214.2 ± 48.4	0.66
Isovolumic relaxation time, ms	84.1 ± 18.0	84.3 ± 16.4	0.94
Right ventricular systolic pressure (mmHg)	24.9 ± 6.2	24.4 ± 6.4	0.65
LV global longitudinal strain, %	-15.6 ± 2.6	-15.0 ± 2.9	0.11
LV global radial strain, %	32.0 ± 10.4	31.5 ± 11.6	0.75
LV global circumferential strain, %	-27.9 ± 7.7	-27.1 ± 6.0	0.34
LA end diastolic volume, mL	54.2 ± 23.9	56.3 ± 23.0	0.46
LA end systolic volume, mL	21.5 ± 13.7	22.5 ± 12.7	0.55
LA ejection fraction, %	63.7 ± 10.7	61.9 ± 10.2	0.18
LA fractional area change, %	49.0 ± 9.8	47.5 ± 9.3	0.21
LA global longitudinal strain	37.8 ± 17.1	37.8 ± 14.9	1.00
LA reservoir strain, %	39.7 ± 18.2	39.4 ± 15.1	0.87
LA conduit strain, %	22.1 ± 11.5	22.7 ± 10.6	0.65
LA contractile strain, %	17.3 ± 13.1	16.7 ± 9.4	0.65

Echo Parameters	HIV neg (N=97)	PWH (N=180)	P value[a]
LA reservoir strain rate, s^{-1}	1.46 ± 0.77	1.35 ± 0.63	0.17
LA conduit strain rate s^{-1}	-0.96 ± 0.56	-0.96 ± 0.58	0.97
LA contractile strain rate, s^{-1}	-1.46 ± 0.80	-1.34 ± 0.72	0.18

[*] Values are presented as mean ± standard deviation, unless specified otherwise

[a] Bonferroni correction for multiple comparisons, revised for 33 comparisons and desired $\alpha = 0.05$; $p = \frac{\alpha}{N} = \frac{0.05}{33} = 0.0015$

LA, left atrium; LV, left ventricle

Table 3:

Association between HIV infection and diastolic dysfunction[a]

Variable	Odds Ratio, (95% CI)	P-value
Hypertension	1.859 (1.073, 3.222)	0.027
Diabetes	0.823 (0.448, 1.515)	0.53
Age, per 5 years	1.363 (1.140, 1.629)	0.0007
Body mass index, per point	1.038 (0.987, 1.092)	0.12
Hepatitis C status	1.127 (0.697, 1.825)	0.63
HIV status	1.010 (0.606, 1.684)	0.97
Analysis with Propensity Score Weighting*		
Variable	**Odds Ratio point estimate, (95% CI)**	**P-value**
HIV status	1.011 (0.722, 1.414)	0.95
Reservoir strain, per 5% strain	0.915 (0.871, 0.962)	0.0005
Conduit strain, per 5% strain	0.825 (0.761, 0.895)	<0.0001
Contractile strain, per 5% strain	0.970 (0.904, 1.040)	0.39
Reservoir strain rate, per 20% strain/sec	0.865 (0.823, 0.909)	<0.0001
Conduit strain rate, per 20% strain/sec	1.151 (1.081, 1.226)	<0.0001
Contractile strain rate, per 20% strain/sec	1.075 (1.025, 1.126)	0.0027

[a]Multivariate ordinal logistic regression analysis, with and without propensity weighting

*Propensity score weighting analysis was performed with each of the variables used in the propensity score (hypertension, diabetes, age, and BMI) as well as HIV and one of the strain parameters.