Cardiovascular Topics

Right ventricular function in treatment-naïve human immunodeficiency virus-infected patients

Bassey Effiong, Victor Ansa, Joseph Andy, Idongesit Odudu-Umoh, Taiwo Shogade, Aquaowo Udosen, Udeme Ekripko

Abstract

Background: Right ventricular dysfunction carries a poorer prognosis in human immunodeficiency virus (HIV)-positive patients. The objectives of this study were to ascertain the prevalence of right ventricular systolic and diastolic dysfunction, as well as its predictors, in antiretroviral therapy-naïve HIV-positive patients.

Methods: Participants in this cross-sectional, descriptive study comprised 60 HIV-positive patients and 60 HIV-negative controls. All participants had transthoracic echocardiography done to assess right ventricular systolic and diastolic function. The HIV-positive patients had their CD4 counts measured.

Results: The mean age of the study population was 34.63 ± 8.7 years versus that of the controls (34.45 ± 9.40 years) (p = 1.000). Right ventricular systolic dysfunction was found in 11.6% of the HIV-positive patients versus the controls (3.33%, p = 0.166) while right ventricular diastolic dysfunction was found in 15.0% of HIV-positive patients versus the controls (1.7%, p = 0.021). The CD4 count did not contribute to the frequency and degree of right ventricular systolic or diastolic dysfunction.

Conclusion: Right ventricular systolic and diastolic dysfunction was common in treatment-naïve HIV-infected individuals but the frequency and degree were not associated with the CD4 count or other measured parameters.

Keywords: human immunodeficiency virus, treatment naïve, right ventricular function, people living with HIV

Department of Internal Medicine, University of Uyo Teaching Hospital, Uyo, Nigeria
Bassey Effiong, MD, FWACP
Aquaowo Udosen, MB BCh, FWACP
Taiwo Shogade, MB BS, FMCP

Department of Internal Medicine, University of Calabar, Calabar, Nigeria
Victor Ansa, MB BS, FWACP, FACP, FRCP (Lond), vic_ansa@yahoo.com

Department of Internal Medicine, University of Uyo, Uyo, Nigeria
Joseph Andy, MD, FWACP, FMCP, DAB
Idongesit Odudu-Umoh, MBBCH, FWACP
Udeme Ekripko, MBBS, FMCP, PhD

Submitted 29/10/22; accepted 5/6/23
Cardiovasc J Afr 2023; **34**: online publication www.cvja.co.za

DOI: 10.5830/CVJA-2023-031

Human immunodeficiency virus (HIV) infection/acquired immunodeficiency syndrome (AIDS) is a global health crisis with approximately 36 million people affected worldwide.[1] Tragically, younger persons are disproportionately affected. HIV remains an urban epidemic but rural dwellers are not spared. New infections are on the decline, but the total number of people living with human immunodeficiency virus (PLWHIV) are still increasing due to higher treatment coverage and longer lifespan with the advent of antiretroviral therapy (ART).[1,2] Those mostly at risk of infection include intravenous drug users, commercial sex workers and men who have sex with men. However, on the African continent, heterosexual transmission accounts for the majority of cases.[1]

As the number of PLWHIV increases due to increased coverage and availability of ART, the occurrence of non-communicable diseases is also expected to rise in this group of patients.[3] Infection with HIV is associated with different cardiovascular manifestations, ranging from rhythm abnormalities, pericarditis with or without pericardial effusion, myocarditis and cardiomyopathy to coronary artery disease.[4-7]

Cardiovascular diseases have been found to account for a substantial number of deaths among HIV-infected patients in recent times.[8,9] Smith *et al*.[8] found that cardiovascular disease accounted for 11.0% of deaths and was the fourth most common cause of death seen in their study of HIV-positive patients, and was only preceded by AIDS-related deaths (29.0%), non-AIDS-defining cancers (15.0%) and liver disease (13.0%).

Left ventricular (LV) function has however been the focus in most of these studies in PLWHIV.[10-16] Uwanuruochi *et al*.[13] found a prevalence of LV systolic and diastolic dysfunction in ART-naïve patients to be 13.6 and 28.8%, respectively, with LV hypertrophy seen in only 3.0% of patients. The lower prevalence of systolic dysfunction was thought to be due to increased cardiac contractility from anaemia, diarrhoea and dehydration.

Very few studies have assessed right ventricular (RV) function in HIV-positive individuals.[10,17,18] In one study, RV systolic dysfunction was about six times more prevalent than LV systolic dysfunction in HIV patients.[10] Isolated RV dysfunction has also been documented in HIV-positive patients.[17] RV systolic dysfunction has been shown to be independently associated with mortality in congestive heart failure, pulmonary hypertension

and myocardial infarction.[19-21] The same may be the case for HIV-associated cardiovascular disease.

The paucity of data in HIV cohorts may partly be because standards for the evaluation of RV function have only recently been established. The physiological importance of the right ventricle has been underestimated with the right ventricle being considered mainly as a conduit, whereas its contractile performance was thought to be haemodynamically unimportant.[22] However, more recently, its contribution to normal cardiac pump function has been well established, its primary function being the maintenance of adequate pulmonary perfusion pressure under varying circulatory and loading conditions in order to deliver desaturated venous blood to the gas exchange membranes of the lungs. It is also responsible for maintaining a low systemic venous pressure to prevent tissue and organ congestion.[23]

A few studies have looked at RV function in this group of patients [17,18,24,25] This study was therefore aimed at providing data on RV function in people with HIV infection and determining the proportion of ART-naïve HIV-infected individuals with RV dysfunction.

Methods

The study was carried out at the University of Uyo Teaching Hospital (UUTH), Uyo, Akwa Ibom state. Uyo is the capital city of Akwa Ibom state, which is located in the southern coastal part of Nigeria, with a population of 5.5 million people (2016). It is bordered on the east by Cross River state, on the west by Rivers and Abia states, and on the south by the Atlantic Ocean.

Patients were recruited from the HIV clinic sponsored by the President's Emergency Plan for AIDS Relief (PEPFAR) and managed by Family Health International (FHI). The Human Research Ethics Committee of the University of Uyo Teaching Hospital granted ethical approval for this study. Each of the participants gave a written, informed consent. Participation was voluntary.

This was a cross-sectional, descriptive study including HIV-positive patients, diagnosed with double enzyme-linked immunosorbent assay (ELISA) between September 2018 and August 2020, who were yet to commence ART. These included patients who were previously diagnosed or were newly diagnosed and presented to the HIV clinic. The controls were apparently healthy HIV-negative age- and gender-matched volunteers who were recruited within the hospital community (hospital staff, medical/nursing students and patients' relatives). Participants were selected consecutively until the sample size was achieved. Inclusion criteria were: established diagnosis of HIV infection and aged 18 years and above.

Exclusion criteria included HIV-positive patients who had been exposed to antiretroviral drugs, hypertensive subjects (known hypertensive patients currently taking antihypertensive medications or those with blood pressure ≥ 140 mmHg systolic and/or ≥ 90 mmHg diastolic), individuals with a history of congenital heart disease, or diabetes mellitus diagnosed in accordance with the American Diabetic Association (ADA) criteria or patients on antidiabetic drugs.[26] Also excluded were those with impaired fasting glucose levels, pregnant women, patients with at least stage three chronic kidney disease, those with significant ethanol intake (more than 50 g of ethanol per day on most days of the week), individuals with ischaemic heart disease and with significant wall motion abnormality, and those with sickle cell disease or pulmonary tuberculosis.

Relevant history and demographic data were obtained. Participants had detailed examinations (general physical and systemic examination), including anthropometric measurements. The clinical staging was done for each subject using a modified World Health Organisation clinical staging system.

Transthoracic two-dimensional (2D) echocardiography, M-mode and Doppler studies were performed using the Sonoscape S20 echocardiography machine with a 3.5-MHz transducer. Subjects were in the left lateral recumbent position and images were obtained in the parasternal long and short axis, apical, as well as subcostal views.

RV systolic function was assessed using RV tricuspid annular plane systolic excursion (TAPSE) and tissue Doppler-derived tricuspid lateral annular systolic velocity (S′) at the tricuspid annulus. Diastolic function was assessed using the ratio of peak early tricuspid inflow to lateral diastolic velocity of the tricuspid annulus (E/E′) and ratio of peak early tricuspid inflow to peak atrial velocity at the tricuspid annulus (E/A). Cardiac measurements were done using the American Society of Echocardiography (ASE) guidelines of leading-edge to leading-edge as measurement points.[27] The presence of wall motion abnormalities, abnormal valve morphology, as well as congenital heart defects and mural thrombi were also assessed.

For evaluation of RV function, images were obtained in the apical four-chamber view and then by placing an M-mode cursor through the tricuspid annulus and measuring the amount of longitudinal motion of the annulus at peak systole. The M-mode cursor was parallel to the tricuspid annulus plane and measurements were taken at the end of expiration. Abnormal values were determined based on the ASE guidelines.[24] Systolic dysfunction was present if TAPSE was < 16 mm (< 1.6 cm) and S′ was < 10 cm/s.

Diastolic dysfunction was diagnosed based on a tricuspid E/A ratio, E/e′ and a diastolic flow predominance in the hepatic veins. E/A < 0.8 was indicative of impaired relaxation (grade I diastolic dysfunction). Tricuspid E/A ratio of 0.8–2.1 with an E/e′ ratio > 6 and a diastolic flow predominance in the hepatic veins was indicative of pseudo-normal filling (grade II diastolic dysfunction). A tricuspid E/A ratio > 2.1 with deceleration time < 120 ms was indicative of restrictive filling (grade III diastolic dysfunction).

Pulmonary artery systolic pressure (PASP) was estimated from the peak tricuspid regurgitation (TR) velocity, using the simplified Bernoulli equation and combining this value with an estimate of the right atrial (RA) pressure.

$RVSP = 4(V)^2 + RA\ pressure,$

where V is the peak velocity (m/s) of the tricuspid valve regurgitant jet. RA pressure was estimated from inferior vena cava (IVC) diameter in peak expiration and the presence of inspiratory collapse.

The subcostal view was used for imaging the IVC, with the IVC viewed in its long axis. The measurement of the IVC diameter was done at end-expiration and just proximal to the junction of the hepatic veins, which lie approximately 0.5–3.0 cm proximal to the ostium of the right atrium.

To assess IVC collapse, the changes in diameter of the IVC with a sniff and with quiet respiration were measured. IVC ≤ 2.1 cm that collapsed more than 50.0% with a sniff suggests a

normal RA pressure of 3 mmHg (range 0–5 mmHg), whereas an IVC diameter > 2.1 cm that collapsed less than 50.0% with a sniff suggests a high RA pressure of 15 mmHg (range 10–20 mmHg). In indeterminate cases in which the IVC diameter and collapse did not fit this paradigm, an intermediate value of 8 mmHg (range 5–10 mmHg) was used.

TR velocity > 2.8–2.9 m/s, corresponding to a PASP of approximately 36 mmHg, assuming an RA pressure of 3–5 mmHg, indicated elevated RV systolic and pulmonary artery (PA) pressure.[24]

All the HIV-positive participants had blood samples taken for measurement of CD4 count.

Statistical analysis

WINPEPI (PEPI-for-Windows) was used for data analysis. Continuous data are presented as means ± standard deviation if normally distributed or as median ± interquartile range if skewed. Means were compared using the student's *t*-test or its non-parametric equivalent (Mann–Whitney *U*-test). Categorical data are reported as frequencies and percentages. Differences between categorical variables were assessed using the chi-squared test or Fisher's exact test if 25% of the cells in the chi-squared table had values less than five.

Univariate analysis and multivariable logistic regression models were used to determine independent associations with RV dysfunction. All variables with a *p*-value of Wald statistics ≤ 0.25 at the univariate level and those with biological plausibility of predicting the outcome (such as age) were fed into the multivariate model. The level of statistical significance was fixed at $p < 0.05$.

Results

A total of 120 participants who met the inclusion criteria were recruited. These comprised 38 (31.7%) males and 82 (68.3%) females. The mean age of the study population was 34.54 ± 9.02 years with a range of 18–56 years. There was no significant difference between the mean age of HIV-positive patients (34.63 ± 8.70 years) and that of the controls (34.45 ± 9.40 years) (p = 1.000). More HIV-positive patients were unemployed (12, 20.0%) compared to the controls (6, 10.0%), 11 HIV patients (18.3%) were engaged in unskilled jobs versus no controls (0.0%) ($p < 0.001$) and 68 patients and controls were single (56.7%). Other sociodemographic characteristics of the study population are summarised in Table 1.

Clinical, biochemical and anthropometric parameters of the study participants are shown in Table 2. The average weight of the controls was significantly higher than that of the HIV patients (73.12 ± 11.80 vs 60.30 ± 12.7 kg, $p < 0.001$). The body mass index (BMI) and body surface area (BSA) of the controls (27.21 ± 4.77 kg/m², 1.82 ± 0.16 m²) were also significantly higher than those of the patients (23.18 ± 5.17 kg/m², 1.64 ± 0.18 m²) ($p < 0.001$). Systolic and diastolic blood pressures were significantly higher in the controls (119 ± 0.16 mmHg, 80.03 ± 7.65 mmHg) compared to those of the HIV patients (114.07 ± 13.30 mmHg, 75.77 ± 9.14 mmHg) ($p = 0.024$, $p = 0.007$). The HIV group had significantly higher pulse rates (84.81 ± 14.99 beats/min) than the controls (74.28 ± 8.73 beats/min) ($p < 0.001$).

The total cholesterol level was significantly higher in the control group than in the patients (4.92 ± 4.57 vs 3.67 ± 0.95 mmol/l, $p = 0.040$), in addition to the controls having significantly higher high-density lipoprotein (HDL) cholesterol levels (1.47 ± 0.43 vs 1.19 ± 0.59 mmol/l, $p = 0.004$). The atherogenic ratio was however comparable in both groups (4.24 ± 4.25 vs 3.66 ± 3.12, $p = 0.396$).

The packed cell volume was significantly lower in the HIV group (32.97 ± 21%) compared to the controls (39.92 ± 4.96%) ($p < 0.001$) but the patients had significantly higher neutrophil counts (47.38 ± 16.52 vs 40.92 ± 9.37 cells/µl, $p = 0.010$). Their

Table 1. Sociodemographic characteristics of the study participants

Variables	*Total,* n *(%)* (n = *120*)	*HIV+ve,* n *(%)* (n = *60*)	*Controls,* n *(%)* (n = *60*)	χ^2/t	p-*value*
Age (years)	34.54 ± 9.02	34.63 ± 8.70	34.45 ± 9.40	0.11	0.913
Female	82 (68.33)	41 (68.33)	41 (68.33)	0.00	1.000
Male	38 (31.67)	19 (31.67)	19 (31.67)		
Occupation					
Skilled	91 (75.83)	37 (61.67)	54 (90.00)	20.48	< 0.001
Unskilled	11 (9.17)	11 (18.33)	0 (0.00)		
Unemployed	18 (15.00)	12 (20.00)	6 (10.00)		
Marital status					
Single	68 (56.67)	34 (56.67)	34 (56.67)	9.10	0.028*
Married	46 (38.33)	20 (33.33)	26 (43.33)		
Separated	2 (1.67)	2 (3.33)	0 (0.00)		
Widow	4 (3.33)	4 (6.67)	0 (0.00)		
Educational status					
No formal education	1 (0.83)	1 (1.67)	0 (0.00)	62.03	< 0.001*
Primary	15 (12.50)	15 (25.00)	0 (0.00)		
Secondary	35 (29.17)	29 (48.33)	6 (10.00)		
Tertiary	69 (57.50)	15 (25.00)	54 (90.00)		

χ^2: chi-squared, *t*: student's *t*-test, *Fisher's exact test.

Table 2. Clinical, biochemical and anthropometric characteristics of study participants

Variables	*Total* (n = *60*) *Mean ± SD*	*HIV+ve* (n = *60*) *Mean ± SD*	*Controls* (n = *60*) *Mean ± SD*	t-*test*	p-*value*
Weight (kg)	66.71 ± 13.82	60.30 ± 12.74	73.12 ± 11.80	–5.72	< 0.001
Height (m)	1.63 ± 0.08	1.62 ± 0.07	1.64 ± 0.82	–0.19	0.851
BMI (kg/m²)	25.20 ± 5.35	23.18 ± 5.17	27.21 ± 4.77	–4.44	< 0.001
BSA (m²)	1.73 ± 0.19	1.64 ± 0.18	1.82 ± 0.16	–5.79	< 0.001
WC (cm)	86.27 ± 9.75	83.68 ± 9.30	88.85 ± 9.58	–3.00	0.003
HC (cm)	100.36 ± 11.06	96.87 ± 11.06	103.85 ± 10.43	–3.56	0.001
WHR	0.86 ± 0.64	0.86 ± 0.08	0.85 ± 0.05	0.82	0.413
SBP (mmHg)	116.65 ± 12.06	114.07 ± 13.30	119 ± 10.16	–2.28	0.024
DBP (mmHg)	77.90 ± 8.66	75.77 ± 9.14	80.03 ± 7.65	–2.77	0.007
PP (mmHg)	37.92 ± 8.65	37.53 ± 10.25	38.30 ± 6.74	–0.47	0.628
MAP (mmHg)	90.81 ± 9.05	88.53 ± 9.57	93.10 ± 7.94	–2.85	0.005
PR (beat/min)	79.50 ± 13.28	84.81 ± 14.99	74.28 ± 8.73	4.70	< 0.001
Total cholesterol (mmol/l)	4.29 ± 3.34	3.67 ± 0.95	4.92 ± 4.57	–2.07	0.040
Triglycerides (mmol/l)	1.15 ± 1.04	1.01 ± 0.72	1.30 ± 1.28	–1.53	0.129
HDL-C (mmol/l)	1.33 ± 0.53	1.19 ± 0.59	1.47 ± 0.43	–2.97	0.004
LDL-C (mmol/l)	2.27 ± 2.44	1.94 ± 0.87	2.59 ± 3.32	1.45	0.149
VLDL-C (mmol/l)	0.60 ± 0.58	0.55 ± 0.40	0.65 ± 0.72	–0.94	0.349
Atherogenic ratio	3.95 ± 3.72	4.24 ± 4.25	3.66 ± 3.12	0.85	0.396

χ^2: chi squared, *t*: student's *t*-test, *Fisher's exact, significant values in bold. HIV+ve: human immunodeficiency virus positive, BSA: body surface area, BMI: body mass index, WC: waist circumference, HC: hip circumference, WHR: waist–hip ratio, SBP: systolic blood pressure, DBP: diastolic blood pressure, PP: pulse pressure, MAP: mean arterial pressure, PR: pulse rate, HDL-C: high-density lipoprotein cholesterol, LDL-C: low-density lipoprotein cholesterol, VLDL-C: very low-density lipoprotein cholesterol.

Table 3. Haematological parameters of study participants

Variables	Total (n = 120) Mean ± SD	HIV+ve (n = 60) Mean ± SD	Control (n = 60) Mean ± SD	t-test	p-value
PCV (%)	36.45 ± 7.08	32.97 ± 7.21	39.92 ± 4.96	–6.15	< 0.001
WBC (cells/µl)	4.81 ± 1.63	4.85 ± 1.88	4.76 ± 1.34	0.30	0.763
Neutrophils (cells/µl)	44.15 ± 13.76	47.38 ± 16.52	40.92 ± 9.37	2.63	0.010
Lymphocytes (cells/µl)	41.17 ± 14.02	37.61 ± 14.77	44.72 ± 12.36	–2.86	0.005
Platelets (cells/µl)	214.82 ± 69.73	228.17 ± 73.22	201.47 ± 63.91	2.13	0.035

HIV+ve: human immunodeficiency virus positive, PCV: packed cell volume, WBC: white blood cell count.

lymphocyte count was lower than that of the controls (37.61 ± 14.77 vs 44.72 ± 12.36 cells/µl, $p = 0.005$ (Table 3).

RV systolic function determined by TAPSE shows a reduced function in the HIV patients compared to the controls (2.07 ± 0.28 vs 2.45 ± 0.28 cm, $p < 0.001$), whereas, using the tricuspid S′, the RV systolic function appeared comparable in the two groups (12.9 ± 11.78 vs 12.50 ± 2.78, $p = 0.338$), as shown in Table 4. RV systolic dysfunction was found in seven (11.67%) of the HIV patients and two (3.33%) of the controls ($p = 0.166$). RV diastolic dysfunction was more common in the HIV patients compared to the controls (9, 15.0% vs 1, 1.67%, $p = 0.021$) and of these, five patients (8.33%) had grade I, two (6.67%) had grade II and none had grade III diastolic dysfunction (Table 5).

The CD4 count did not contribute to the frequency and degree of diastolic dysfunction, as shown in Table 6.

Table 7 shows the logistic regression model for predictors of RV dysfunction in the HIV patients. Univariate as well as multivariate regression models were used to determine factors that predicted the occurrence of RV dysfunction in the HIV patients. All variables with a p-value of the Wald statistics ≤ 0.25 at univariate level and those with biological plausibility of predicting outcome (in this case, age) were fed into the multivariate model. None of the variables (increasing age, gender, low-density lipoprotein cholesterol levels, triglycerides, CD4 count and mean arterial pressure could independently predict RV dysfunction in the group. The area under the receiver operating characteristic curve of this model was 0.75 (Fig. 1).

Discussion

RV diastolic dysfunction was present in 15% of our HIV-positive treatment-naïve subjects and therefore it was significantly more common in them compared to the seronegative controls. Lacomis *et al.*[25] found a near-similar percentage of RV diastolic dysfunction (11.0%) in their own study of HIV-positive patients. RV systolic dysfunction did not vary significantly between the HIV-positive cohort and the controls. These findings are similar to results documented in LV studies where diastolic dysfunction appeared to predominate, most likely due to increased LV mass.[12,15]

RV dysfunction may have been due to the frequent pulmonary infections encountered in PLWHIV.[28] Frequent pulmonary infections may lead to changes in the pulmonary vasculature: intimal proliferation and smooth muscle cell hypertrophy, which may subsequently lead to cardiac dysfunction.[29]

The physiological importance of the right ventricle has been underestimated, with it being considered mainly as a conduit, whereas its contractile performance was thought to be haemodynamically unimportant.[22] However, its essential contribution to normal cardiac pump function is now well established, its primary functions being maintenance of adequate pulmonary perfusion pressure under varying circulatory and loading conditions in order to deliver desaturated venous blood to the gas-exchange membranes of the lungs, as well as maintaining a low systemic venous pressure to prevent tissue and organ congestion.[23]

Although a few studies have looked at RV function in PLWHIV, none has demonstrated clear associations.[18,25,30] This

Table 4. Echocardiographic parameters of the study participants

Variables	Total (n = 120) Mean + SD	HIV+ve (n = 60) Mean + SD	Controls (n = 60) Mean + SD	t-test	p-value
TAPSE (cm)	2.26 ± 0.33	2.07 ± 0.25	2.45 ± 0.28	–7.84	< 0.001
Tricuspid S′ (cm/s)	12.70 ± 2.33	12.50 ± 2.78	12.91 ± 1.78	–0.96	0.338
Tricuspid E (cm/s)	47.22 ± 8.53	48.23 ± 9.29	46.21 ± 7.64	1.30	0.196
Tricuspid A (cm/s)	37.99 ± 11.76	41.23 ± 14.12	34.75 ± 7.64	3.13	0.002
Tricuspid E/A	1.29 ± 0.29	1.26 ± 0.34	1.33 ± 0.24	–1.30	0.195
TRV max (cm/s)	93.30 ± 33.80	101.99 ± 37.60	84.61 ± 27.14	2.90	0.004
RA pressure (mmHg)	5.32 ± 4.02	7.13 ± 4.86	3.50 ± 1.51	5.53	< 0.001
PASP (mmHg)	9.10 ± 6.14	11.68 ± 7.40	6.51 ± 2.75	5.07	< 0.001

t: student's t test, HIV+ve: human immunodeficiency virus positive, TASPE: tricuspid annular systolic plane excursion, RA: right atrium, PASP: pulmonary artery systolic pressure.

Table 5. Frequency of RV dysfunction

Variables	Total (n = 120)	HIV+ve (n = 60)	Control (n = 60)	χ^2	p-value
RV diastolic dysfunction, *n* (%)	10 (8.33)	9 (15.00)	1 (1.67)	5.35	0.021*
Grade I		5 (8.33)			
Grade II		4 (6.67)			
Grade II		0 (0.00)			
Right ventricular systolic dysfunction, *n* (%) (TAPSE < 1.6 cm)	9 (7.50)	7 (11.67)		1.92	0.166

TASPE: tricuspid annular systolic plane excursion, HIV: human immunodeficiency virus. *Fisher's exact, significant values in bold.

Table 6. RV diastolic function of HIV patients in relation to CD4 count

Variables	≤ 200 cells/µl (n = 36)	> 200 cells/µl (n = 24)	χ^2	p-value
RV diastolic dysfunction, *n* (%)				
No RV diastolic dysfunction	29 (80.56)	22 (91.67)		
Grade I	5 (13.86)	0 (0.00)	5.48	0.065*
Grade II	2 (5.56)	2 (8.33)		
Grade III	0 (0.00)	0 (0.00)		

χ^2: chi squared, *Fisher's exact test.

Table 7. Logistic regression model for predictors of RV dysfunction in HIV patients

Variable	Univariate analysis, odds ratio (95% CI)	p-value	Multivariate analysis odds ratio (95% CI)	p-value
Age	1.00 (0.94–1.06)	0.94	1.01 (0.93–1.08)	0.89
Gender	0.28 (0.06–1.43)	0.13	0.28 (0.04–1.73)	0.17
LDL-C	1.67 (0.83–3.35)	0.15	1.40 (0.64–3.10)	0.40
Triglycerides	0.40 (0.12–1.30)	0.13	0.44 (0.10–1.85)	0.27
CD4 count	0.97 (0.93–1.02)	0.23	0.97 (0.92–1.03)	0.30
Mean arterial pressure	1.05 (.98–1.13)	0.19	1.06 (0.97–1.14)	0.19

CI: confidence interval, LDL-C: low-density lipoprotein cholesterol. Area under the receiver operating curve of this model was 0.75.

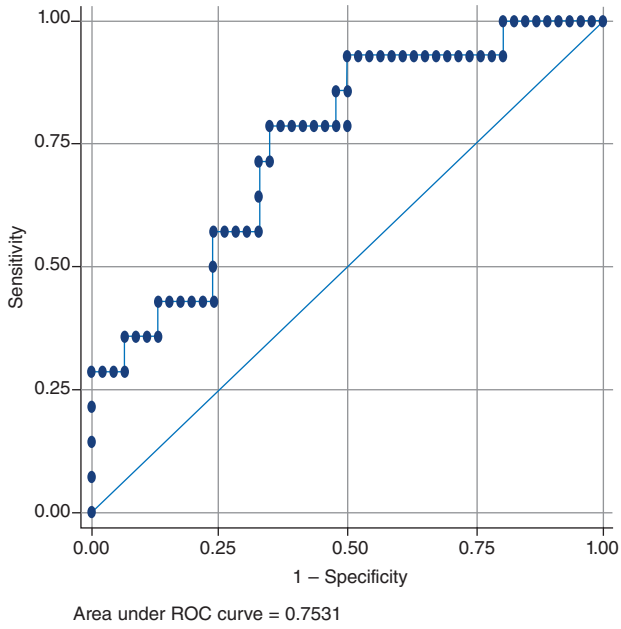

Fig. 1. Receiver operating characteristic curve of the logistic regression model.

may be as a result of the small number of subjects with RV dysfunction reported in the studies, making further analysis of results difficult. RV dysfunction is associated with increased morbidity and mortality rates in patients with congestive cardiac failure and myocardial infarction,[20,21] therefore it may be important in determining the long-term quality of life and survival in PLWHIV with cardiovascular disease.

This study showed that the CD4 count did not contribute to the frequency and degree of diastolic dysfunction. Studies on the effect of CD4 count on RV function are rare. However, studies relating CD4 count to LV function abound but with variable results.[14,31] Adebola *et al.*, in their study of LV function in treatment-naïve HIV patients, reported that LV systolic and diastolic function were more affected in patients with low CD4 counts of ≤ 200 cells/µl,[31] while Ogunmodede *et al.*,[14] in their study, could not establish any relationship between disease severity and chamber dimensions in subjects with CD4 counts below and above 200 cells/m^3.

The majority of the HIV-positive study participants were female (68.3%) and the mean age of the participants was 34.54 ± 9.02 years. This is similar to the mean age of 35.7 ± 10.13 years obtained by Mankwe *et al.*[15] This is not surprising, considering the main mode of transmission in sub-Saharan Africa is heterosexual, as most subjects were in their reproductive ages.[32,33]

Gender inequality, unemployment and disempowerment of women may be responsible for the higher proportion of females seen in the study subjects.[34] Domestic violence as well as low socio-economic status have also been seen as factors that promote risky sexual behaviour in sub-Saharan Africa.[35-37] The predominance of females in study populations involving PLWHIV has been documented in previous studies.[13,14]

Our study showed significantly more HIV subjects than controls doing unskilled jobs and a large proportion were unemployed. Stigma and discrimination at the work place, as well as frequent ill-health may be the reason for this.

The significantly lower BMI seen in the HIV-positive subjects is attributable to weight loss, which is a known characteristic of HIV infection. Weight loss may be due to poor intake of food and frequent diarrhoea in PLWHIV. The HIV subjects also had significantly lower systolic and diastolic blood pressures than the controls. The impact of weight loss on blood pressure may be manifesting in the subjects. The mechanism is unclear but a decline in plasma renin activity has been shown to correlate with weight reduction in obese patients placed on a weight-reduction diet, as reported by Tuck *et al.*[38] Weight loss is also associated with less inhibition of natriuretic peptide, leading to fluid loss and vasodilatation.[39] Similar findings have been reported by Ogunmodede *et al.*[14]

The significantly higher pulse rate seen among our study subjects mirrors the symptoms of HIV, especially fever, as well as low packed cell volume, as seen in the patients. Anaemia causes hypoxia due to decreased haemoglobin levels and thus triggers compensatory tachycardia, aimed at improving tissue oxygenation. Anaemia in HIV has different aetiologies, ranging from the suppressive effect of HIV on the bone marrow, recurrent and opportunistic infections, as well as use of Zidovudine in its treatment.[40]

Thrombocytopenia is common in PLWHIV and is attributable to accelerated peripheral platelet destruction by antiplatelet antibodies and insufficient production of platelets from the infected megakaryocytes.[41] Improvement in platelet count upon commencement of ART has been documented.[42] A few studies have documented increased platelet counts in PLWHIV, which has been implicated in thrombotic complications, such as the increased incidence of myocardial infarction seen in HIV patients.[43]

Conclusion

RV diastolic and systolic dysfunction are common among PLWHIV, especially those who are ART-naïve, and appear not to be related to the CD4 cell count. Overall, no predictors of RV dysfunction were identified in this study. Early initial evaluation of the heart in HIV patients is recommended.

References

1. UNAIDS. GlobalAIDSUpdate2016_slides. 2016.
2. May M, Gompels M, Delpech V, Porter K, Post F, Johnson M, *et al.* Impact of late diagnosis and treatment on life expectancy in people with HIV-1: UK Collaborative HIV Cohort (UK CHIC) study. *Br Med J* 2011; 343.
3. Smit M, Brinkman K, Geerlings S, Smit C, Thyagarajan K, Sighem A, *et al.* Future challenges for clinical care of an ageing population infected with HIV: a modelling study. *Lancet Infect Dis* 2015; **15**(7): 810–818.
4. Sakthiv Adivel V, Appandraj S. A study on cardiac abnormalities in HIV patients and its relation with CD4 count and risk factors. *Int Arch Integr Med* 2016; **3**(6): 170–177.
5. Dau B, Holodniy M. The relationship between HIV Infection and cardiovascular disease. *Curr Cardiol Rev* 2008; **4**(3): 203–218.
6. Chastain DB, King TS, Stover KR. Infectious and Non-infectious etiologies of cardiovascular disease in human immunodeficiency virus infection. *Open AIDS J* 2016; **10**(1): 113–126.
7. Thienemann F, Sliwa K, Rockstroh JK. HIV and the heart: the impact of antiretroviral therapy: a global perspective. *Eur Heart J* 2013; **34**: 3538–3546.

8. Smith CJ, Ryom L, Weber R, Morlat P, Pradier C, Reiss P, *et al.* Trends over time in underlying causes of death amongst HIV-positive individuals from 1999 to 2011. *Lancet* 1016; **384**(1014): 241–248.
9. Domingues C-SB, Waldman EA. Causes of death among people living with AIDS in the pre- and post-HAART eras in the city of São Paulo, Brazil. *PLoS One* 2014; **9**(12): e114661.
10. Isasti G, Pérez I, Moreno T, Cabrera F, Palacios R, Santos J. Echocardiographic abnormalities and associated factors in a cohort of asymptomatic HIV-infected patients. *AIDS Res Hum Retroviruses* 2012; **29**(1): 20–24.
11. Hsue PY, Hunt PW, Ho JE, Farah HH, Schnell A, Hoh R, *et al*. Impact of HIV infection on diastolic function and left ventricular mass. *Circ Heart Fail* 2010; **3**(1): 132–139.
12. Longo-Mbenza B, Seghers L V, Kintoki Vita E, Tonduangu K, Bayekula M. Assessment of ventricular diastolic function in AIDS patients from Congo: a Doppler echocardiographic study. *Heart* 1998; **80**: 184–189.
13. Uwanuruochi K, Onwubere B, Anisiuba B. Echocardiographic study of left ventricular function in HIV-infected Nigerians. *West African J Radiol* 2015; **22**(1): 27.
14. Ogunmodede JA, Kolo PM, Katibi IA, Salami AK, Omotoso A. Structural echocardiographic abnormalities seen in HIV/AIDS patients are independent of cd4 count. *Niger J Clin Pract* 2017; **20**(6): 716–723.
15. Chesa Mankwe A, Odia OJ. Association between CD4+ lymphocyte count and left ventricular diastolic function and geometry in newly diagnosed highly active antiretroviral therapy (HAART) naive HIV/AIDS patients seen at University of Port Harcourt Teaching Hospital, Port Harcourt, Rivers. *J Cardiovasc Dis Diagn* 2017; **5**(5).
16. Kofi Owusu I, Oppong B. Echocardiographic abnormalities in patients with HIV infection at Komfo Anokye Teaching Hospital, Ghana. *J Gen Pract* 2014; **2**(02).
17. Simon MA, Lacomis CD, George MP, Kessinger C, Weinman R, McMahon D, *et al.* Isolated right ventricular dysfunction in patients with human immunodeficiency virus. *J Card Fail* 2014; **20**(6): 414–421.
18. Kristoffersen U, Lebech A, Gerstoft J, Hesse B, Petersen C, Gutte H, *et al*. Right and left cardiac function in HIV-infected patients investigated using radionuclide ventriculography and brain natriuretic peptide: a 5-year follow-up study. *HIV Med* 2008; **9**(3): 180–186.
19. Pallin DJ. New bedside predictor of right ventricular dysfunction in acute pulmonary embolism. *N Engl J Med J Watch* 2017; **2017**: NA44025.
20. Ghio S, Gavazzi A, Campana C, Inserra C, Klersy C, Sebastiani R, *et al*. Independent and additive prognostic value of right ventricular systolic function and pulmonary artery pressure in patients with chronic heart failure. *J Am Coll Cardiol* 2001; **37**(1): 183–188.
21. Mehta SR, Eikelboom JW, Natarajan MK, Diaz R, Yi C, Gibbons RJ, *et al.* Impact of right ventricular involvement on mortality and morbidity in patients with inferior myocardial infarction. *J Am Coll Cardiol* 2001; 37(1): 37–43.
22. Starr I, Jeffers WA, Meade RH. The absence of conspicuous increments of venous pressure after severe damage to the right ventricle of the dog, with a discussion of the relation between clinical congestive failure and heart disease. *Am Heart J* 1943; **26**(3): 291–301.
23. Bleeker GB, Steendijk P, Holman ER, Yu C-M, Breithardt OA, Kaandorp TAM, *et al.* Assessing right ventricular function: the role of echocardiography and complementary technologies. *Heart* 2006; **92**(Suppl 1): i19–26.
24. Rudski LG, Lai WW, Afilalo J, Hua L, Handschumacher MD, Chandrasekaran K, *et al.* Guidelines for the echocardiographic assessment of the right heart in adults: a report from the American Society of Echocardiography. Endorsed by the European Association of Echocardiography, a registered branch of the European Society of Cardiology. *J Am Soc Echocardiogr* 2010; **23**(7): 685–713.
25. Lacomis CD, Morris AM, Patricia George M, Simon MA. Right ventricular dysfunction in HIV. *J Card Fail* 2012; **18**(8): S66.
26. American Diabetes Association. 2. Classification and diagnosis of diabetes. *Diabetes Care* 2016; **39**(Suppl 1): S13–22.
27. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, *et al*. Recommendations for Cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr* 2015; **28**(1): 1–39.
28. Gingo MR, Morris A. Pathogenesis of HIV and the lung. *Curr HIV/AIDS Rep* 2013; **10**(1): 42–50.
29. MeiLan K. Han, MD M, Vallerie V. McLaughlin M, Gerard J. Criner M, Fernando J. Martinez, MD M. Cardiovascular involvement in general medical conditions pulmonary diseases and the heart. *Circulation* 2007; **116**(25): 2992–3005.
30. Erqou S, Lodebo BT, Masri A, Altibi AM, Echouffo-Tcheugui JB, Dzudie A, *et al.* Cardiac dysfunction among people living with HIV: a systematic review and meta-analysis. *J Am Coll Cardiol Heart Fail* 2019; **7**(2): 98–108.
31. Adebola A, Akinbo A, Daniel F. Relationship between CD4 cell count and left ventricular dimension and function in treatment-naïve human immunodeficiency virus-infected patients. *Niger J Cardiol* 2019; **16**(1): 11.
32. Alary M, Lowndes CM, Thompson L. The central role of clients of female sex workers in the dynamics of heterosexual HIV transmission in sub-Saharan Africa. *AIDS* 2004; **18**(6): 945–947.
33. Kharsany ABM, Karim QA. HIV infection and AIDS in sub-Saharan Africa: current status, challenges and opportunities. *Open AIDS J* 2016; **10**: 34–48.
34. Klaas NE, Thupayagale-Tshweneagae G, Makua TP. The role of gender in the spread of HIV and AIDS among farmworkers in South Africa. *Afr J Prim Healtth Care Fam Med* 2018; **10**(1).
35. Wathuta J. Gender inequality dynamics in the prevention of a heterosexual HIV epidemic in sub-Saharan Africa. *Afr J AIDS Res* 2016; **15**(1): 55–66.
36. Wojcicki JM. Socioeconomic status as a risk factor for HIV infection in women in East, Central and southern Africa: a systematic review. *J Biosoc Sci* 2005; **37**(1): 1–36.
37. Jewkes RK, Dunkle K, Nduna M, Shai N. Intimate partner violence, relationship power inequity, and incidence of HIV infection in young women in South Africa: a cohort study. *Lancet* 2010; **376**(9734): 41–48.
38. Tuck ML, Sowers J, Dornfeld L, Kledzik G, Maxwell M, Sowers J. The effect of weight reduction on blood pressure, plasma renin activity, and plasma aldosterone levels in obese patients. *N Engl J Med* 1981; **304**(16): 930–933.
39. Reisin E, Frohlich ED. Effects of weight reduction on arterial pressure. *J Chronic Dis* 1982; **35**(12): 887–891.
40. Masaisa F, Gahutu JB, Mukiibi J, Delanghe J, Philippé J. Anemia in human immunodeficiency virus-infected and uninfected women in Rwanda. *Am J Trop Med Hyg* 2011; **84**(3): 456–460.
41. Sundell I, Koka P. Thrombocytopenia in HIV infection: impairment of platelet formation and loss correlates with increased c-Mpl and ligand thrombopoietin expression. *Curr HIV Res* 2005; **4**(1): 107–116.
42. Nascimento FG, Tanaka PY. Thrombocytopenia in HIV-infected patients. *Indian J Hematol Blood Transfus* 2012; **28**(2): 109–111.
43. Mayne E, Funderburg NT, Sieg SF, Asaad R, Kalinowska M, Rodriguez B, *et al*. Increased platelet and microparticle activation in HIV infection: upregulation of P-selectin and tissue factor expression. *J Acquir Immune Defic Syndr* 2012; **59**(4): 340–346.