# Isolated Right Ventricular Dysfunction in Patients With Human Immunodeficiency Virus

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## ABSTRACT

**Background:** HIV-infected individuals are at increased risk for pulmonary hypertension and cardiomyopathy, portending a poor prognosis. Right ventricular (RV) dysfunction is associated with worse outcomes in these conditions, yet its prevalence is poorly defined in HIV. We sought to determine the prevalence of RV dysfunction in an outpatient HIV cohort.

**Methods:** Echocardiograms were evaluated from 104 HIV-infected adults. Measurements included estimated pulmonary arterial systolic pressure (PASP) and several measures of RV function, including tricuspid annular plane systolic excursion (TAPSE), RV longitudinal myocardial strain (RVLMS), RV fractional area change (RVFAC), and myocardial performance index (MPI).

**Results:** Sixteen subjects (15%) had PASP $>35$ mm Hg, yet RV function did not differ significantly from those with normal estimated PASP. RV dysfunction defined by RVFAC $<35\%$ occurred in 11%. RVLMS had a median value of $-27.3\%$, and individuals below the median had lower TAPSE but no differences in left ventricular ejection fraction (LVEF), PASP, or other measures. Dyspnea was associated with the lowest quintile of RVLMS ($\geq -21.05\%$). There were 6 subjects with LVEF $<50\%$, and these individuals had lower TAPSE but no differences in PASP or other RV functional measures.

**Conclusions:** RV dysfunction was common as estimated PASP $>35$ mm Hg and LV dysfunction, but these findings did not cosegregate. RV dysfunction in HIV-infected individuals may be a separate entity from LV/global cardiomyopathy or pulmonary hypertension and deserves further study. (*J Cardiac Fail 2014;20:414–421*)

**Key words:** Pulmonary hypertension, HIV, right ventricle, cardiomyopathy.

Human immunodeficiency virus (HIV) infection has been associated with many cardiac abnormalities, including cardiomyopathy, pulmonary hypertension (PH), and coronary artery disease.[1–4] In contrast, the presence and nature of right ventricular (RV) abnormalities have not been extensively studied. Although isolated RV dysfunction in HIV was reported in 2 studies 20 years ago, the severity of RV dysfunction has not been documented in the current era except for 1 report using radionuclide ventriculography.[3–5] That report found isolated RV dysfunction in 5% of HIV patients. In addition, echocardiographic technology has advanced considerably, and several new measures of RV function have since been validated. Because RV dysfunction is linked to increased

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mortality in PH[6,7] and most cardiac diseases,[8−11] understanding of RV function in HIV is important prognostically and, potentially, therapeutically.

Assessment of ventricular function is critical in the evaluation of PH because left ventricular (LV) dysfunction may cause PH, and RV function is at risk in PH.[12] Assessment of ventricular function is particularly important in HIV-associated PH because of the wide range of cardiac abnormalities associated with HIV.[1−4] Although it is possible to use echocardiography to screen for PH, diagnosis requires invasive measurement of hemodynamics, because recent studies have found that echocardiographic measures in HIV may under- or overdiagnose PH in this population.[13] Additionally, diagnosis is typically delayed up to several years, frequently not until the disease has reached later stages including RV dilation and dysfunction.[14,15] Whether echocardiographic examination of the RV could add to diagnosis of PH in HIV-infected individuals is unknown.

The objectives of the present study were to define the prevalence of RV dysfunction in an outpatient HIV cohort with the use of current-era echocardiographic technology and to determine the association of RV dysfunction with echocardiographic signs of PH and left-sided heart failure.

## Methods

### Study Setting

Participants in an ongoing prospective multicenter study of lung and cardiac function in HIV were prospectively enrolled in this echocardiographic substudy at our center only. Details of this study have been previously published.[16,17] Briefly, inclusion criteria were documented HIV infection and attendance at the University of Pittsburgh HIV/acquired immunodeficiency syndrome clinic. Individuals were excluded if they were experiencing new or increasing respiratory symptoms or fevers within the preceding 4 weeks. Participants in this substudy underwent echocardiography between September 16, 2009, and May 31, 2011. The protocol was approved by the University of Pittsburgh Institutional Review Board, and every participant signed written informed consent. Demographic and clinical data were collected by participant interview and medical record review. Laboratory studies were obtained from the medical record and included the most recent CD4+ T-lymphocyte cell count and plasma HIV RNA level within 3 months. The lower limit of detection for the HIV RNA polymerase chain reaction assay was 50 copies/mL. Antiretroviral therapy (ART) use was defined as use of ≥3 antiretroviral agents from ≥2 classes of medications in the preceding 3 months.

### Transthoracic Echocardiography

Echocardiography was performed with a GE-Vingmed Vivid 7 system (GE Vingmed Ultrasound, Horten, Norway). From standard 2-dimensional views, pulsed- and continuous-wave Doppler measurements were obtained according to the American Echocardiography Association recommendations.[18,19] The examination was recorded digitally. All studies were read by 1 investigator (CDL) and reviewed by an experienced cardiologist (MAS); any disagreements were reviewed by both readers and measures jointly agreed upon. RV end-diastolic (RVEDA) and end-systolic (RVESA) areas were measured from the apical 4-chamber view to calculate RV fractional area change [RVFAC = (RVEDA − RVESA)/RVEDA) × 100].[20] Peak pulmonary arterial systolic pressures (PASPs) were estimated by calculating the systolic pressure gradient between the RV and RA by the maximum velocity of the tricuspid regurgitant jet with the use of the modified Bernoulli equation, and then adding to this gradient an estimated right atrial pressure based on the size of the inferior vena cava and its variation with respiration.[21] LV ejection fraction (LVEF) was calculated via the biplane Simpson method. Tricuspid annular systolic plane excursion (TAPSE) was measured by M-mode of the lateral tricuspid valve annulus.[22] Myocardial performance index (MPI) was calculated as the ratio of the time of the isovolumic phases of the cardiac cycle to ejection time as derived from Doppler imaging of the RV inflow and outflow in the parasternal short axis.[23] Eccentricity index was calculated as the ratio of LV diameter parallel to the septal wall plane to LV diameter perpendicular to the septal wall plane.[24]

Strain analysis by speckle tracking was performed by tracing the endocardial RV surface in the apical 4-chamber view (mean frame rate 77 ± 17/s) with the use of a point-and-click approach with special care taken to adjust tracking of all endocardial segments (EchoPAC; GE Vingmed Ultrasound). A second larger concentric border was then automatically generated and manually adjusted near the epicardium. Speckle tracking automatically analyzed frame-by-frame movement of the stable patterns of natural acoustic markers, or speckles, over the cardiac cycle. The location shift of these acoustic markers representing tissue movement provided spatial and temporal data used to calculate regional strain vectors as change in length/initial length, with myocardial thickening along the longitudinal axis considered to be positive. The image was then automatically divided into 6 standard segments with corresponding time-strain curves from each segment. Strain values were reported for the middle and basal regions of the RV free wall.

### Statistical Analyses

Variables of RV function that were evaluated included the following: RVFAC, TAPSE, MPI, eccentricity index, and longitudinal myocardial strain of the middle and basal RV free wall (RVLMS). To evaluate the effect of PH on RV function, individuals were stratified by an estimated PASP (derived from the echocardiogram) of 35 mm Hg, which has been used to define mild PH.[25] To evaluate the effect of speckle tracking−derived longitudinal myocardial strain of the RV on other measures of RV function, participants were stratified by a value of −27.3%, which was the median of the cohort. To evaluate the effect of TAPSE on other measures of RV function, participants were stratified by a value of 2.2 cm, which was the lowest quartile of the cohort. To evaluate the effect of LV function on measures of RV function, we stratified by an LVEF value of 50%. Participants were also stratified by whether or not they were receiving ART. Variables were evaluated for normal distribution. Between-group differences were calculated with the use of the independent-sample Student t-test or the Mann-Whitney test for normally and nonnormally distributed variables, respectively, or Pearson chi-square for categoric variables. Data are expressed as mean ± SD. Statistical significance was defined as a 2-sided $P$ value of $<.05$. All statistical calculations were made with the use of SPSS for Windows (version 20; SPSS, Chicago, Illinois).