Effect of Left Ventricular Dysfunction and Viral Load on Risk of Sudden Cardiac Death in Patients With Human Immunodeficiency Virus

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Human immunodeficiency virus (HIV)−infected patients are disproportionately affected by cardiovascular disease and sudden cardiac death (SCD). Whether left ventricular (LV) dysfunction predicts SCD in those with HIV is unknown. We sought to determine the impact of LV dysfunction on SCD in patients with HIV. We previously characterized all SCDs and acquired immunodeficiency syndrome (AIDS) deaths in 2,860 consecutive patients in a public HIV clinic from 2000 to 2009. Transthoracic echocardiograms (TTEs) performed during the study period were identified. The effect of ejection fraction (EF), diastolic dysfunction, pulmonary artery pressure, and LV mass on SCD and AIDS death were evaluated: 423 patients had at least 1 TTE; 13 SCDs and 55 AIDS deaths had at least 1 TTE. In the propensity-adjusted analysis, EF 30% to 39% and EF <30% predicted SCD (hazard ratio [HR] 9.5, 95% confidence interval [CI] 1.7 to 53.3, p = 0.01 and HR 38.5, 95% CI 7.6 to 195.0, p <0.001, respectively) but not AIDS death. Diastolic dysfunction also predicted SCD (HR 14.8, 95% CI 4.0 to 55.4, p <0.001) but not AIDS death, even after adjusting for EF. The association between EF <40% and SCD was greater in subjects with detectable versus undetectable HIV RNA (adjusted HR 11.7, 95% CI 2.9 to 47.2, p = 0.001 vs HR 2.7, 95% CI 0.3 to 27.6, p = 0.41; p = 0.07 for interaction). In conclusion, LV systolic dysfunction and diastolic dysfunction predict SCD but not AIDS death in a large HIV cohort, with greater effect in those with detectable HIV RNA. Further investigation is needed to thoroughly evaluate the effect of low EF and HIV factors on SCD incidence and the potential benefit of implantable cardioverter-defibrillator therapy in this high-risk population. **(Am J Cardiol 2014;113:1260−1265)**

We recently determined that sudden cardiac deaths (SCDs) composed the majority of cardiac deaths over a 10-year period in a large, urban, human immunodeficiency virus (HIV)−positive cohort, at an adjusted rate 4.5-fold higher than expected.[1] In the general population, left ventricular (LV) systolic dysfunction is strongly associated with an increased risk of SCD,[2−4] but this association has not been evaluated in the setting of HIV infection. Because most deaths in large HIV cohorts are still acquired immunodeficiency syndrome (AIDS) related,[5,6] whether LV dysfunction carries the same prognostic importance for HIV-infected subjects is unknown. In addition, HIV-infected subjects may be at risk for ventricular arrhythmias by mechanisms independent of LV systolic dysfunction, including QT interval prolongation,[7−9] inflammation,[10] and direct viral effects on cardiomyocyte depolarization and repolarization.[11,12] We therefore sought to evaluate any potential association between premortem LV dysfunction and SCD and AIDS-related death in a large urban cohort of HIV-infected patients.

Methods

We previously identified records of 2,860 consecutive patients monitored at a public HIV clinic at San Francisco General Hospital from April 1, 2000 to August 31, 2009.[1] This clinic serves approximately 20% of HIV-infected patients in San Francisco. For this analysis, we included all patients aged ≥18 years with documented HIV infection who had at least 1 transthoracic echocardiogram (TTE) during this period. The study was approved by the Institutional Review Board of the University of California, San Francisco.

We previously identified and classified all deaths in this cohort.[1] Briefly, SCDs were defined as meeting 2 published criteria: (1) primary International Classification of Diseases, tenth revision, code for all cardiac causes[13,14] and (2)

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Table 1
Comparison of baseline characteristics

Characteristic	All Subjects With TTE (n = 423)	SCD (n = 13)	AIDS Death (n = 55)	p Value*
Mean age (yrs)	42.3 ± 9.4	43.6 ± 10.8	41.2 ± 8.6	0.39
Women	80 (19)	1 (8)	10 (18)	0.36
Body mass index (kg/m^2)	25.0 ± 5.2	27.0 ± 6.9	24.4 ± 5.3	0.52
Race/ethnicity				0.38
African-American	147 (35)	8 (62)	23 (42)	
Asian American	14 (3)	0	1 (2)	
European American	174 (41)	5 (38)	21 (38)	
Hispanic American	83 (20)	0	10 (18)	
Other	5 (1)	0	1 (2)	
CAD	24 (6)	1 (8)	1 (2)	0.26
MI	13 (3)	0	1 (2)	0.62
HTN	101 (24)	4 (31)	9 (16)	0.21
Smoking	113 (27)	2 (15)	11 (20)	0.52
Diabetes mellitus	38 (9)	1 (8)	5 (9)	0.67
Chronic kidney disease	46 (11)	2 (15)	8 (15)	0.62
Illicit drug use	128 (30)	2 (15)	14 (25)	0.44
Medications				
ACE inhibitor	66 (16)	1 (8)	11 (20)	0.30
β Blocker	64 (15)	1 (8)	7 (13)	0.61
Statin	51 (12)	1 (8)	2 (4)	0.52
NRTI	260 (61)	6 (46)	39 (71)	0.09
NNRTI	138 (32)	3 (23)	17 (31)	0.58
PI	229 (54)	5 (38)	32 (58)	0.20
CD4 count (cells/mm^3)†	274 (89−458)	310 (268−534)	111 (35−278)	0.003
HIV RNA (log copies/ml)†	3.7 (1.9−4.8)	3.6 (2.3−4.0)	4.5 (1.9−5.3)	0.09

Values are mean ± SD, n (%), or median (interquartile range).
ACE = angiotensin-converting enzyme; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor.
* p Value for comparison between SCDs and AIDS deaths.
† Most recent measurement.

Table 2
Transthoracic echocardiogram characteristics

Characteristic	All Subjects (n = 423)	SCD (n = 13)	AIDS Death (n = 55)	p Value*
Left ventricular ejection fraction (%)				
>50	339/423 (80)	3/13 (23)	45/55 (82)	<0.0001
40−50	39/423 (9)	4/13 (31)	5/55 (9)	0.04
30−39	29/423 (7)	3/13 (23)	4/55 (7)	0.09
<30	16/423 (4)	3/13 (23)	1/55 (2)	0.003
Diastolic dysfunction†	29/299 (10)	5/8 (63)	1/38 (3)	<0.0001
PASP (mm Hg)	27.0 (21−33)	29.5 (22−42)	27.0 (23−33)	0.28
Pulmonary HTN‡	100/314 (32)	4/13 (31)	13/55 (24)	0.59
LV hypertrophy	127/420 (30)	3/13 (23)	20/53 (38)	0.32

Values are n/total assessed (%) or median (interquartile range).
* p Value for comparison between SCDs and AIDS deaths.
† Stage II and III diastolic dysfunction.
‡ PASP >30 mm Hg.

circumstances of death meeting World Health Organization criteria for SCD (death within 1 hour of symptom onset if witnessed or within 24 hours of being observed alive and symptom-free if unwitnessed)[15] or unexpected out-of-hospital death.[16] Hospice, overdose, violence, suicide, cancer, or opportunistic infection deaths were excluded. All unexpected deaths classified as SCD were confirmed as not meeting criteria for AIDS death. AIDS death required 2 of 3 published criteria: (1) primary International Classification of Diseases, tenth revision, code for HIV disease−related illness, (2) circumstances of death involving HIV-related infection or illness, or (3) most recent CD4 cell count of <50 cells/mm^3.[6]

Baseline characteristics were abstracted from the clinic's electronic medical record. We recorded the following variables: age, gender, race, CD4 cell count, HIV viral load, antiretroviral medication use, cardiac medication use, coronary artery disease (CAD), hypertension (HTN), diabetes mellitus, smoking, disorders of lipid metabolism, chronic kidney disease, and illicit drug use.