

Incidence, Predictors, and Outcomes of Implantable Cardioverter-Defibrillator Discharge Among People Living With HIV

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Background—People living with HIV (PHIV) are at an increased risk for sudden cardiac death, and implantable cardioverter-defibrillators (ICDs) prevent SCD. There are no data on the incidence, predictors, and effects of ICD therapies among PHIV.

Methods and Results—We compared ICD discharge rates between 59 PHIV and 267 uninfected controls. For PHIV, we tested the association of traditional cardiovascular risk factors and HIV-specific parameters with an ICD discharge and then tested whether an ICD discharge among PHIV was associated with cardiovascular mortality or an admission for heart failure. The indication for ICD insertion was similar among groups. Compared with controls, PHIV with an ICD were more likely to have coronary artery disease and to use cocaine. In follow-up, PHIV had a higher ICD discharge rate (39% versus 20%; $P=0.001$; median follow-up period, 19 months). Among PHIV, cocaine use, coronary artery disease, QRS duration, and higher New York Heart Association class were associated with an ICD discharge. An ICD discharge had a prognostic effect, with a subsequent 1.7-fold increase in heart failure admission and a 2-fold increase in cardiovascular mortality, an effect consistent across racial/ethnic and sex categories.

Conclusions—ICD discharge rates are higher among PHIV compared with uninfected controls. Among PHIV, cocaine use and New York Heart Association class are associated with increased ICD discharge, and an ICD discharge is associated with a subsequent increase in admission for heart failure and cardiovascular mortality. (*J Am Heart Assoc.* 2018;7:e009857. DOI: 10.1161/JAHA.118.009857.)

Key Words: heart failure • HIV • implantable cardioverter-defibrillator discharge • implantable cardioverter-defibrillator

People living with HIV (PHIV) are at a 4.5-fold increased risk for sudden cardiac death (SCD).¹ The mechanisms involved in the increase in SCD in PHIV are incompletely understood but are likely related, in part, to the increase in the prevalence of heart failure (HF) and coronary artery disease (CAD).^{2–4} For example, PHIV taking antiretroviral

therapy (ART) experience rates of incident HF that are 50% to 200% higher than matched uninfected controls.^{5–7} Implantable cardioverter-defibrillators (ICDs) are a standard intervention for both the primary and secondary prevention of SCD.^{8,9} However, despite the increased risk of SCD among PHIV and the established role of ICDs in preventing SCD in appropriate patients, there are limited contemporary data on the use of ICDs among PHIV. Data before the era of effective ART suggested that PHIV during that period were less likely to receive an ICD because of shorter lifespans or concerns related to infectious complications.¹⁰ These concerns are largely resolved, and current studies suggest a lower risk of infectious complications.^{11,12} Therefore, the aim of this study was to add to the limited data on the incidence, predictors, and outcomes of an ICD discharge among PHIV.¹³

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Accompanying Tables S1 through S4 are available at <https://www.ahajournals.org/doi/suppl/10.1161/JAHA.118.009857>

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Methods

Study Design and Patient Population

After obtaining Institutional Board Review approval, we created a registry of all patients admitted to a single academic center in 2011 with decompensated HF (Bronx-Lebanon Hospital Center of Icahn School of Medicine at

Clinical Perspective

What Is New?

- Implantable cardioverter-defibrillator discharge rates are higher among people living with HIV with heart failure compared with uninfected controls with heart failure.
- The increased rates of implantable cardioverter-defibrillator discharge were associated with higher use of cocaine among people living with HIV.
- Implantable cardioverter-defibrillator discharge among people living with HIV was associated with markedly increased heart failure hospitalization and cardiovascular mortality.

What Are the Clinical Implications?

- The people living with HIV and heart failure are at increased arrhythmia risk, and future studies are warranted in this high-risk group.

Mount Sinai, Bronx, NY). The requirement for obtaining the consent was waived. The primary aim of the registry was to compare outcomes and predictors of HF outcomes among PHIV and controls. From this registry, we identified those patients with an ICD. The diagnosis of HIV as well as other clinically relevant variables were ascertained through manual review of each of the individual electronic health records (EHRs). The requests for data, analytic methods, and study materials availability to other researchers for purposes of reproducing the results or replicating the procedure will be considered.

Covariates

Baseline data were collected from EHRs from the time of the index HF hospitalization. These data included the following: the presence of hypertension, dyslipidemia, diabetes mellitus, CAD, family history of CAD, body mass index, left ventricular ejection fraction, prior or active cigarette smoking, and prior or active cocaine use. Medication use was recorded from the date of discharge from the index HF hospitalization. HIV-specific parameters (CD4 cell count, viral load, ART, and duration of therapy) were recorded from those available closest to the time of discharge from the index HF hospitalization.

Outcomes

The follow-up period began on the date of discharge from the index HF hospitalization in 2011. The outcome of interest was an ICD discharge that was classified as appropriate if the intervention was a result of ventricular tachyarrhythmia, per established criteria.^{14,15} If the device delivered the first therapy for a sustained ventricular arrhythmia, it was considered

appropriate therapy; and if the therapy was delivered for a supraventricular arrhythmia or for an episode of oversensing, it was considered inappropriate therapy. We also obtained data on antitachycardia pacing (ATP). Review of ICD data was performed at 3- to 6-month intervals via clinic visits or through transmitted ICD data by a board-certified electrophysiologist. The interpretation of the ICD data was derived from the EHR and was not independently reviewed. We next tested the effect of an ICD discharge on subsequent cardiovascular mortality and repeated HF admission among PHIV. The effect of an ICD discharge on subsequent cardiovascular mortality and repeated HF admission was tested among all PHIV and stratified by sex, race, and ethnicity. Cardiovascular mortality was defined as death attributable to HF, SCD, arrhythmias, and acute ischemic events.¹⁶ Death was determined through the Social Security Death Index, and cause of death was confirmed by physician-adjudicated individual EHR review. An HF admission was ascertained through physician-adjudicated individual EHR review using previously defined criteria.¹⁷ The HF readmission was after ICD discharge for individuals who experienced ICD discharge and was from index hospitalization for patients who did not experience an ICD discharge.

Statistical Analysis

Continuous variables were presented as mean and SD or median (interquartile range), based on normality, and categorical variables were presented as percentages. Continuous data were compared using unpaired Student *t* tests or Wilcoxon rank-sum tests, as appropriate. Categorical data were compared using the χ^2 or the Fisher exact test. Survival curves were plotted using Kaplan-Meier curves. Univariate analyses were performed to determine the association between covariates and ICD discharge. The CD4 cell count was included as a continuous variable, and the viral load was included as a binary variable (suppressed, <200 copies/mL; or nonsuppressed, ≥ 200 copies/mL). Because CD4 cell count and viral suppression are colinear, CD4 cell count only was included in the model. Exact logistic regression was then used to screen covariates for their association with the outcome. Covariates with bivariate $P < 0.01$ were considered for inclusion in the multivariable logistic regression models. Statistical significance was otherwise defined using a 2-tailed $P < 0.05$. Statistical analyses were performed using SAS, version 9.4, statistical software.

Results

Demographics and Characteristics

The entire study cohort consisted of 2578 patients admitted in 2011 with HF. The final study group included 353

individuals with an ICD, of which 27 (7%) were observed in a different hospital or lost to follow-up, and therefore were excluded from the final data analysis. Of the 326 individuals with HF and ICD with follow-up, 59 were PHIV and 267 were uninfected controls. Among PHIV, 81% (48/59) were prescribed ART, and the median duration of ART prescription was 9 years (interquartile range, 4–16 years). The mean CD4 cell count was 238 cells/mm³; 53% (199/374) had a CD4 cell count of ≥ 200 cells/mm³, and 51% (30/59) had a viral load of < 200 copies/mL. People with and without HIV did not differ with respect to age, sex, race/ethnicity, or the prevalence of diabetes mellitus, hypertension, and cigarette smoking (Table 1). The type of ICD (single chamber, dual chamber, or cardiac resynchronization therapy), the indication for ICD (ie, primary or secondary prevention), the left ventricular ejection fraction, and the use of antiarrhythmic medications were also similar between PHIV and controls (Table 1). However, the pulmonary artery systolic pressure (46 ± 12.8 versus 40 ± 9.9 mm Hg; $P=0.03$), the prevalence of hyperlipidemia (61% versus 40%; $P=0.004$), background rates of CAD (68% versus 42%; $P<0.001$), and cocaine use (47% versus 25%; $P<0.001$) were higher among PHIV (Table 1).

ICD Therapy

The mean detection rate triggering shock therapies was 217 beats per minute, and most of the ICD and cardiac resynchronization therapy devices were programmed to zone 2 or zone 3 therapies (81%). The median follow-up duration was 19 months (interquartile range, 3–24 months). Among the entire cohort ($n=326$), 147 patients (45%) received an ICD therapy (ICD discharge or ATP), 83 patients (23%) had an ICD discharge (13% with an appropriate discharge and 10% with an inappropriate discharge), and 85 patients (22%) had ATP (11% with an appropriate ATP and 11% with an inappropriate ATP). When compared, PHIV had a higher ICD discharge rate and ATP compared with uninfected controls (Table 2). On univariate analysis, cocaine use, a history of CAD, higher New York Heart Association class, longer QRS duration, a lower left ventricular ejection fraction, and a lower CD4 cell count were associated with ICD discharge among PHIV (Table 3). On exact logistic regression analysis, cocaine use, history of CAD, higher New York Heart Association class, and QRS duration remained predictors of an ICD discharge among PHIV (Table 4) in a model inclusive of CD4 cell count.

The Effect of ICD Discharge on Subsequent Cardiovascular Events Among PHIV

Among PHIV, we tested the effect of an ICD discharge on subsequent cardiovascular mortality and 30-day HF admission/readmission. Cardiovascular mortality and HF admission

rates were higher among those PHIV whose ICD discharged compared with PHIV whose ICD did not discharge (cardiovascular mortality: 74% versus 33% [$P=0.01$]; and 30-day HF admission: 83% versus 52% [$P=0.01$]; Figure 1). Within PHIV, we also separately tested the effects of an appropriate discharge, inappropriate ICD discharge, and ATP on cardiovascular mortality and 30-day readmission. An appropriate ICD discharge was associated with higher cardiovascular mortality as well as a higher 30-day HF admission rate compared with no discharge (cardiovascular mortality: 92% versus 33% [$P<0.001$]; and 30-day HF admission rate: 100% versus 52% [$P<0.001$]; Figure 2). There was no statistically significant difference in cardiovascular mortality as well as HF admission rate among PHIV when those with and without an inappropriate ICD discharge (cardiovascular mortality: 50% versus 33% [$P>0.05$]; HF admission rate: 60% versus 52% [$P>0.05$]; Figure 3) and those with and without ATP (cardiovascular mortality: 40% versus 33% [$P>0.05$]; 30-day HF admission rate: 53% versus 52% [$P>0.05$]; Figure 4) were compared. The effect of an ICD discharge on adverse outcomes was similar when stratified by sex, ethnicity, and race. For example, among men and women with HIV, an ICD discharge was associated with a higher cardiovascular mortality (men, 88% versus 50% for discharge versus no discharge [$P=0.02$]; women, 83% versus 30% for discharge versus no discharge [$P=0.02$]). Similar findings were noted among blacks and Hispanics with HIV, in whom an ICD discharge was associated with a higher subsequent cardiovascular mortality (blacks, 87% versus 31% for discharge versus no discharge [$P=0.02$]; Hispanics, 86% versus 25% for discharge versus no discharge [$P=0.02$]) (Figure 5).

On univariate analysis, cocaine use, a history of CAD, higher New York Heart Association class, QRS duration, a low left ventricular ejection fraction, and a lower CD4 cell count were associated with ICD discharge (Table S1). On exact logistic regression analysis, cocaine use, appropriate ICD discharge, history of CAD, use of β blockers, higher New York Heart Association class, and QRS duration were predictors of cardiovascular mortality (Table S2).

Similar to the findings among PHIV, cardiovascular mortality and HF admission rates were higher among those non-HIV individuals whose ICD discharged compared with those whose ICD did not discharge (cardiovascular mortality: 58% versus 22% [$P=0.001$]; and 30-day HF admission, 68% versus 39% [$P=0.001$]). Within the non-HIV group, we also separately tested the effects of an appropriate discharge, an inappropriate ICD discharge, and ATP on cardiovascular mortality and 30-day readmission. An appropriate ICD discharge was associated with higher cardiovascular mortality and 30-day HF admission rate compared with no discharge (cardiovascular mortality: 79% versus 22% [$P<0.001$]; and 30-day HF admission rate: 85% versus 39% [$P<0.001$]). There was no

Table 1. Baseline Characteristics of PHIV With ICD vs Non-HIV Controls With ICD

Characteristics	PHIV (n=59)	Non-HIV Controls (n=267)	P Value
Female sex	26 (44)	108 (40)	0.609
Age, y	61±9.5	60±9.4	0.886
Ethnicity			
Hispanic	23 (39)	112 (42)	0.883
Black	21 (36)	93 (35)	
Others	15 (25)	61 (23)	
Cardiovascular risk factors			
Diabetes mellitus	29 (49)	109 (40)	0.241
Hypertension	43 (72)	176 (66)	0.303
Hyperlipidemia	36 (61)	108 (40)	0.004*
Smoking	35 (59)	136 (51)	0.253
LVEF, %	31±13.7	33±14.9	0.636
PASP, mm Hg	46±12.8	40±9.9	0.030*
Systolic BP, mm Hg	135±26.8	138±27.6	0.448
Diastolic BP, mm Hg	74±18.6	76±19.1	0.465
Heart rate, bpm	83±22.2	79±21.4	0.198
QRS duration, ms	117±25.3	113±26.6	0.293
QTc duration, ms	455±30.6	449±31.8	0.188
Serum creatinine, mg/dL	1.33±1.0	1.28±1.1	0.748
BMI, kg/m ²	26±5.1	28±5.5	0.185
Sleep apnea	16 (27)	65 (24)	0.655
Chronic lung disease	17 (28)	59 (22)	0.269
CAD	40 (68)	113 (42)	<0.001*
NYHA class			0.565
I/II	26 (44)	131 (49)	
III/IV	33 (56)	136 (51)	
Cocaine use	28 (47)	66 (25)	<0.001*
Mode of cocaine administration			
Intranasal	8 (30)	22 (33)	
Smoking	11 (39)	28 (43)	0.723
Intravenous	9 (32)	16 (24)	
HIV parameters			
CD4 cell count/mm ³	238±192		
VL <200 copies/mL	30 (51)		
ART	48 (81)		
Duration of therapy, median (IQR), y	9 (4–16)		
HF medications			
β Blocker	48 (81)	227 (85)	0.483
ACEI/ARB	47 (80)	235 (88)	0.090

Continued

Table 1. Continued

Characteristics	PHIV (n=59)	Non-HIV Controls (n=267)	P Value
Spironolactone	35 (59)	158 (60)	0.984
Furosemide	47 (80)	199 (75)	0.407
Antiarrhythmic medications	30 (51)	164 (61)	0.134
Amiodarone	13 (22)	70 (26)	
Dofetilide	9 (15)	51 (19)	
Sotalol	8 (13)	43 (16)	
ICD parameters			
Primary prevention	46 (78)	189 (71)	0.265
Secondary prevention	13 (22)	78 (29)	0.265
Single-chamber ICD	27 (46)	119 (45)	0.857
Dual-chamber ICD	23 (39)	113 (42)	
CRT-D	9 (15)	35 (13)	
Zone 2 or 3 programming	48 (82)	216 (81)	0.935
Prior ICD discharge or ATP	12 (20)	45 (17)	0.524
History of device infection	3 (5.1)	3 (1.1)	0.146
ICD implantation during index HF admission	5 (8.5)	19 (7)	0.717

Data are given as number (percentage) or mean±SD, unless otherwise indicated. ACEI indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ART, antiretroviral therapy; ATP, antitachycardia pacing; BMI, body mass index; BP, blood pressure; bpm, beats per minute; CAD, coronary artery disease; CRT-D, cardiac resynchronization therapy defibrillator; HF, heart failure; ICD, implantable cardioverter-defibrillator; IQR, interquartile range; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; PASP, pulmonary artery systolic pressure; PHIV, people living with HIV; VL, viral load.

QTc interval is the corrected measure of time between the onset of ventricular depolarization and completion of repolarization. (Corrected QT interval).

*Statistically significant *P*-value.

statistically significant difference in cardiovascular mortality as well as HF admission rate among the non-HIV group when those with and without an inappropriate ICD discharge (cardiovascular mortality: 33% versus 22% [*P*>0.05]; HF admission rate: 46% versus 39% [*P*>0.05]), and those with and without ATP (cardiovascular mortality: 25% versus 22% [*P*>0.05]; 30-day HF admission rate: 42% versus 39% [*P*>0.05]; Table S3), were compared. While comparing PHIV with an ICD prescribed ART with those not prescribed ART, a trend was observed with a higher ICD therapy rate as well as cardiovascular mortality and 30-day HF readmission rate among PHIV with an ICD not prescribed ART (Table S4).

Discussion

We analyzed a registry of patients admitted with HF in a geographical area with a high background prevalence of HIV to characterize outcomes and predictors of outcomes among PHIV with an ICD. Our analyses yielded several key findings:

Table 2. ICD Therapy in PHIV vs Non-HIV Controls

Variable	PHIV (N=59)	Non-HIV Controls (N=267)	P Value
ICD therapy			0.001
ICD discharge	23 (39)	53 (20)	
ATP	15 (26)	56 (21)	
Type of ICD therapy			0.007
Appropriate ICD discharge	13 (22)	29 (11)	
Appropriate ATP	9 (15)	26 (10)	
Inappropriate ICD discharge	10 (17)	24 (9)	
Inappropriate ATP	6 (10)	30 (11)	
Type of ICD discharge			0.657
Appropriate discharge (n=13)			
VF	7 (54)	12 (41)	
VT	6 (46)	17 (59)	
Inappropriate discharge (n=10)			
Afib/flutter	7 (70)	12 (50)	
SVT	3 (30)	9 (38)	
Abnormal sensing	0	3 (12)	

Data are given as number (percentage). Afib indicates atrial fibrillation; ATP, antitachycardia pacing; ICD, implantable cardioverter-defibrillator; PHIV, people living with HIV; SVT, supraventricular tachycardia; VF, ventricular fibrillation; VT, ventricular tachycardia.

(1) Compared with uninfected controls with an ICD, PHIV were more likely to have CAD and to use cocaine. (2) PHIV had almost double the ICD discharge rate compared with uninfected patients; this increase was seen for both an appropriate and an inappropriate ICD discharge. (3) Cocaine use among PHIV was a strong predictor of an ICD discharge. (4) Among PHIV, an appropriate ICD discharge was associated with a subsequent increase in cardiovascular mortality and HF admission. (5) The effect of an ICD discharge on subsequent cardiovascular mortality was consistent when stratified by sex, ethnicity, and race.

Tseng and colleagues reported a 4-fold increase in SCD among PHIV.¹ This increased risk of SCD among PHIV in that study was associated with a diagnosis of HF or a cardiomyopathy. An ICD discharge is a surrogate for the risk for SCD. In findings that are supportive of those from Tseng and colleagues,¹ we report that ICD discharge rates were almost 2-fold higher among PHIV. The mechanisms involved in the increase in ICD discharge among PHIV have not been fully elucidated. Myocardial fibrosis may play a key role; it is a key pathophysiological driver for the development of cardiac arrhythmias, and both the presence and the extent of myocardial fibrosis are predictors of ventricular arrhythmias.^{15,18–20} At baseline, PHIV without HF have both an increase in the presence and extent of myocardial fibrosis.^{21,22}

Table 3. Univariate Analysis: Predictors of ICD Discharge Among PHIV

ICD Discharge	Hazard Ratio	95% CI		P Value
		Lower	Upper	
Sex	1.086	0.608	1.940	0.778
Age	0.989	0.936	1.046	0.704
BMI	1.010	0.912	1.118	0.853
Diabetes mellitus	1.104	0.652	1.869	0.711
Hypertension	1.406	0.561	3.522	0.458
Hyperlipidemia	1.460	0.712	2.993	0.282
Smoking	1.081	0.694	1.684	0.726
H/o CAD	1.790	1.487	2.056	0.008*
Cocaine	2.190	1.133	4.237	0.007*
LVEF	0.955	0.915	0.996	0.030
PASP	1.023	0.979	1.069	0.304
SA	1.323	0.919	1.906	0.097
Viral load	1.054	0.875	1.270	0.559
CD4 cell count	0.996	0.992	0.998	0.009*
ART duration	0.935	0.806	1.084	0.373
β Blocker	0.627	0.504	0.885	0.010*
ACEI/ARB	0.894	0.322	2.484	0.831
Spirolactone	0.639	0.349	1.170	0.151
Furosemide	0.894	0.322	2.484	0.831
Antiarrhythmics	0.785	0.564	2.012	0.463
QRS duration	1.456	1.110	1.872	0.003*
QTc duration	1.094	0.872	1.284	0.226
Higher NYHA class	1.812	1.122	2.446	0.002*

ACEI indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ART, antiretroviral therapy; BMI, body mass index; CI, confidence interval; H/o CAD, history of coronary artery disease; ICD, implantable cardioverter-defibrillator; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; PASP, pulmonary artery systolic pressure; PHIV, people living with HIV; SA, sleep apnea. QTc interval is the corrected measure of time between the onset of ventricular depolarization and completion of repolarization. (Corrected QT interval). * $P < 0.05$.

For example, Holloway and colleagues detected late gadolinium enhancement, replacement myocardial fibrosis on MRI, in 76% of PHIV compared with 13% of controls.²¹ In a complementary study, Thiara and colleagues found an increased extent of diffuse myocardial fibrosis among PHIV.²³ In addition, our cohort had HF, CAD, and increased rates of cocaine use, all of which are also associated with an increase in both the presence and extent of myocardial fibrosis.^{24,25} For example, late gadolinium enhancement has been reported in >30% of patients with a nonischemic cardiomyopathy and >80% of patients with an ischemic cardiomyopathy.²⁵ Cocaine use leads to heightened sympathetic tone,²⁶ blocks sodium channels,²⁶ and can lead to myocardial fibrosis.²⁴ The use of cocaine may also affect

Table 4. Multivariate Analysis: Predictors of ICD Discharge Among PHIV

ICD Discharge Outcome	Hazard Ratio	95% CI		P Value
		Lower	Upper	
H/o CAD	1.312	1.028	1.716	0.010*
Cocaine	1.214	1.016	1.828	0.011*
CD4 cell count	0.992	0.864	1.112	0.124
β Blockers	0.721	0.453	0.985	0.023*
QRS duration	1.243	1.061	1.437	0.008*
Higher NYHA class	1.371	1.007	1.753	0.010*

Exact logistic regression for multivariate analysis for ICD discharge. This model included all the covariates with $P < 0.05$ on univariate analysis (Table 3). CI indicates confidence interval; H/o CAD, history of coronary artery disease; ICD, implantable cardioverter-defibrillator; NYHA, New York Heart Association; PHIV, people living with HIV. *Statistically significant P -value.

the prescription of standard HF medications, which reduce the burden of ventricular arrhythmias. Specifically, β blockers, a standard treatment for HF and SCD prevention, are occasionally held when cocaine use is suspected.^{27,28} In this cohort, β blockers were prescribed in >80% of individuals with HIV and among 86% of cocaine users. In the context of high rates of ART prescription and low rates of viral suppression, β-blocker medications played an unclear role in our findings. Moreover, this cohort is from a tertiary care center located in the South Central Bronx, NY. This is a region containing patients from diverse backgrounds but also from lower socioeconomic groups. This region has a high prevalence of illicit drug use and HIV compared with suburban areas with better socioeconomic status. The prevalence of cocaine use in our cohort is

comparable to that reported in other contemporary observational clinical cohort studies from the same region (19%–30% among people without HIV and 40%–50% among PHIV).^{29–31}

During follow-up, an ICD discharge among PHIV had prognostic effects. Specifically, PHIV who had an ICD discharge had increased rates of cardiovascular mortality and 30-day HF admission. These findings of an increase in cardiovascular mortality and HF readmission with an ICD discharge were also noted among traditionally underrepresented groups, such as women, blacks, and Hispanics. In broad populations with an ICD, the cardiovascular mortality and HF readmission rates are reported to range from 15% to 22% and from 20% to 30%, respectively, over a similar duration of follow-up.^{8,32,33} These event rates are similar to those reported in our non-HIV controls. In patients without HIV, repetitive ICD discharges are associated with recurrent hospitalizations, anxiety, and depression, and, whether appropriate or inappropriate, lead to a 2- to 5-fold increase in mortality, with the most common cause being HF.^{34–36} This is compounded in this study population because individuals with HIV and HF have been previously demonstrated to have an increased risk at baseline of progressive HF.⁷ Specifically, women with PHIV and HF were reported to have a rate of HF hospitalization 2.5 times that of uninfected controls with HF.⁷ This increased rate of hospitalization was also noted to occur in association with an increased rate of cocaine use. Cocaine use is additionally important herein, as detailed previously, because it also increases the defibrillation threshold,^{24,37} leading to a reduced likelihood of response to a standard ICD discharge and an increase in mortality.

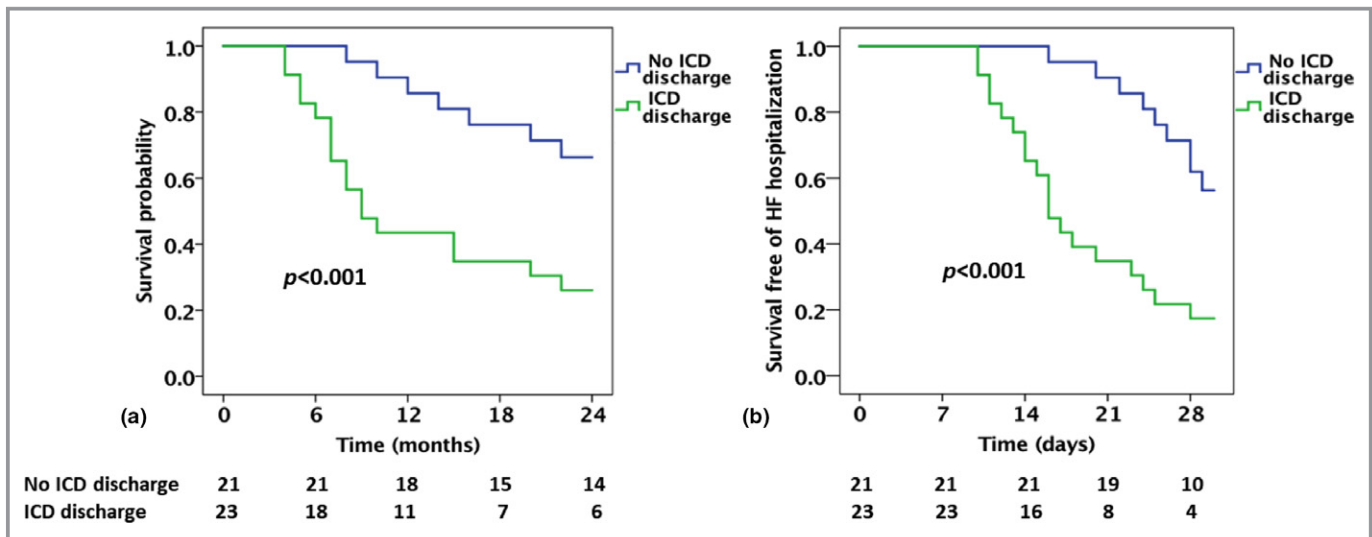


Figure 1. Kaplan-Meier survival curves comparing cardiovascular mortality (A) and 30-day heart failure readmission (B) among people living with HIV admitted with heart failure who have an implantable cardioverter-defibrillator (ICD) with ICD discharge (appropriate or inappropriate) vs no ICD discharge.

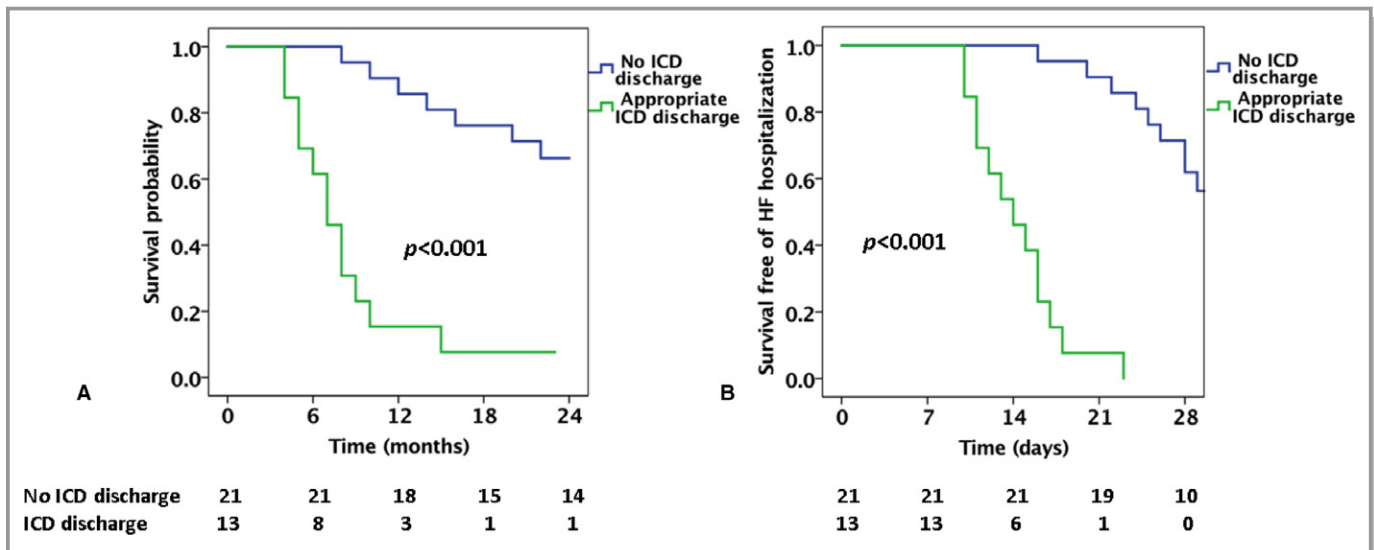


Figure 2. Kaplan-Meier survival curves comparing cardiovascular mortality (A) and 30-day heart failure readmission (B) among people living with HIV admitted with heart failure who have an implantable cardioverter-defibrillator (ICD) with appropriate ICD discharge vs no ICD discharge.

There are limitations of this study that may affect the generalizability and interpretation of our findings. First, the cohort is a group of patients who were admitted to the hospital for acute decompensated HF; therefore, this is a population with a higher risk than a stable outpatient HF cohort and, perhaps, a population of ICD patients without HF. Second, a larger sample size with longer follow-up and more events may allow examination of additional associations with ICD discharge, including CD4 cell count or viral load. Therefore, it is unclear if, among PHIV with higher rates of viral suppression, the ICD discharge rate would be as high. Furthermore, the

overall viral suppression rate in this study was 51%. This rate of viral suppression is comparable to other contemporary observational clinical cohort studies (suppression rates of 45%–62%)^{1,5,38} and studies in this region (viral suppression rate of 58%),³⁹ but is lower than observed in more recent registries and clinical trials.^{40–42} It is also possible that the PHIV with an ICD were sicker for other reasons, such as concomitant infections/lower CD4 cell count, and therefore more likely to have an ICD discharge. There are no comparative prior data on ICD discharge among PHIV; however, we can compare our findings from the uninfected control group to

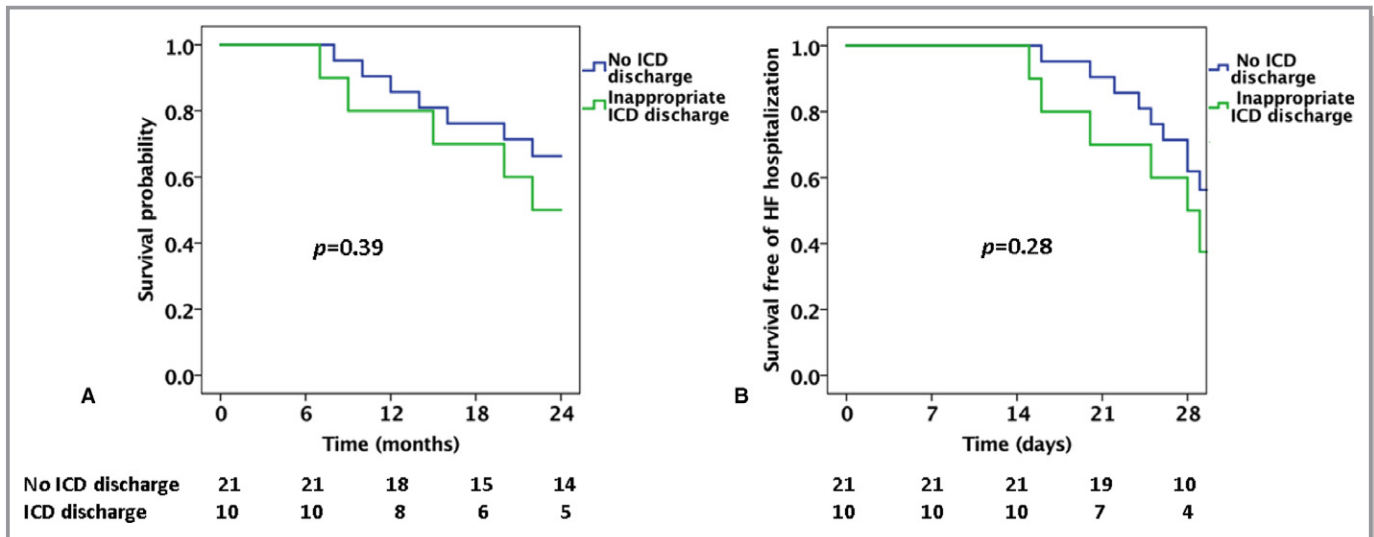


Figure 3. Kaplan-Meier survival curves comparing cardiovascular mortality (A) and 30-day heart failure readmission (B) among people living with HIV admitted with heart failure who have an implantable cardioverter-defibrillator (ICD) with inappropriate ICD discharge vs no ICD discharge.

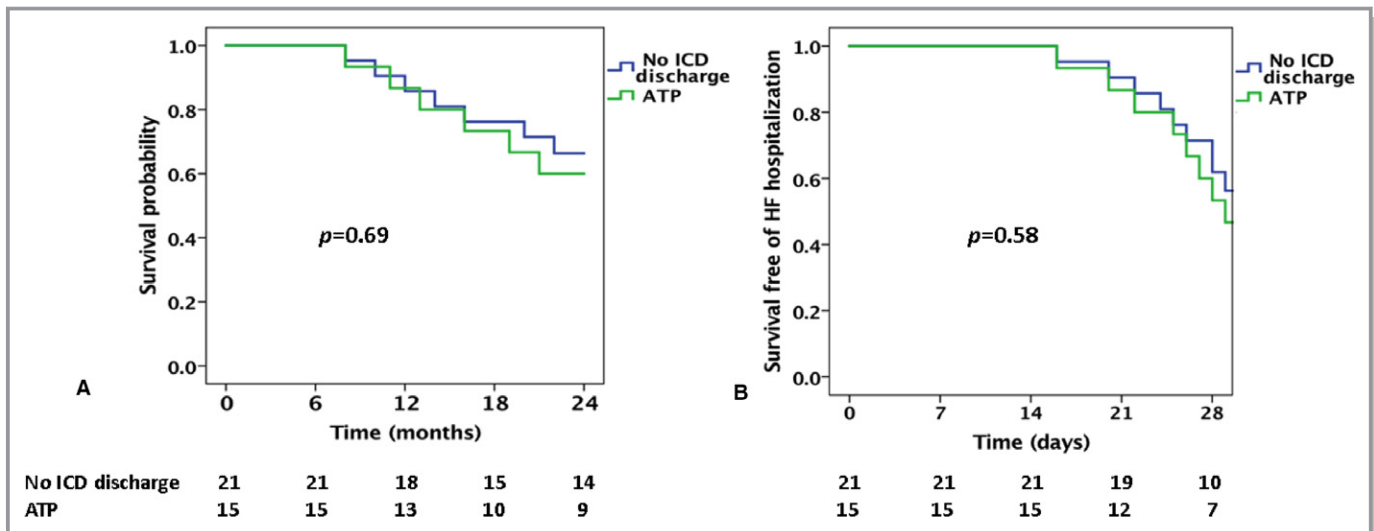


Figure 4. Kaplan-Meier survival curves comparing cardiovascular mortality (A) and 30-day heart failure readmission (B) among people living with HIV admitted with heart failure who have an implantable cardioverter-defibrillator (ICD) with antitachycardia pacing (ATP) vs no ICD discharge.

ICD discharge rates among people without known HIV.⁴³⁻⁴⁵ We noted an ICD discharge rate of 23% among uninfected controls over 19 months of follow-up. This rate of ICD

discharge among our uninfected cohort is modestly higher than published rates among contemporary populations of a similar age. For example, in a study of 194 006 patients with

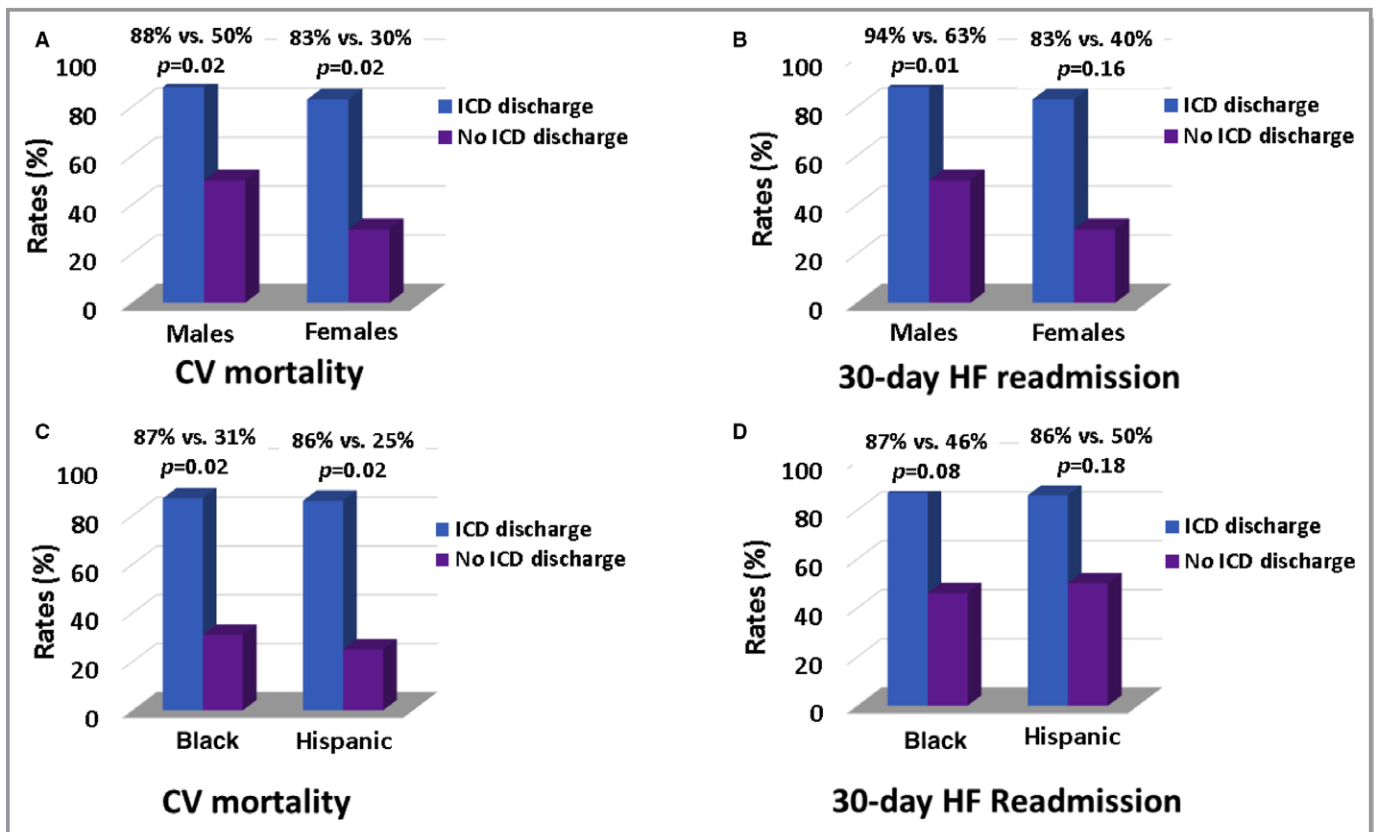


Figure 5. Bar graphs. A, Cardiovascular mortality among men living with HIV vs women living with HIV admitted with heart failure (HF) who have an implantable cardioverter-defibrillator (ICD) with ICD discharge vs no ICD discharge. B, The 30-day HF readmission among men living with HIV vs women living with HIV admitted with HF who have ICD with ICD discharge vs no ICD discharge. C, Cardiovascular mortality among blacks living with HIV vs Hispanics living with HIV admitted with HF who have ICD with ICD discharge vs no ICD discharge. D, The 30-day HF readmission among blacks living with HIV vs Hispanics living with HIV admitted with HF who have ICD with ICD discharge vs no ICD discharge.

an ICD, Saxon and colleagues reported an ICD discharge rate of $\approx 18\%$ over a similar follow-up period.⁴⁴ The mechanisms for the small differences in ICD discharge rate in our presumed uninfected population are unclear but are likely, in part, mediated by a high background prevalence of diabetes mellitus,⁴⁶ cocaine use,²⁶ and the lower rate of cardiac resynchronization therapy use.⁴⁷ Finally, the interpretation of the ICD data was derived from the EHR from the interpretation of a board-certified electrophysiologist and was not independently reviewed.

In conclusion, among PHIV with an ICD, with HF, the rates of ICD discharge are increased compared with those among uninfected controls. The increased rates of ICD discharge may be related, in part, to higher use of cocaine among PHIV. An ICD discharge had an effect on subsequent outcomes among PHIV. Specifically, an ICD discharge among PHIV was associated with markedly increased HF hospitalization and cardiovascular mortality. This population is at increased risk and warrants specific additional strategies to reduce ICD discharge rates. Future studies are required additionally among PHIV with an ICD who have not been hospitalized with HF because those hospitalized with HF represent a higher-risk group.

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Disclosures

None.

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SUPPLEMENTAL MATERIAL

Table S1. Univariate analysis: Factors associated with CV mortality among PHIV with an ICD.

CV mortality outcome	Hazard ratio	95% CI		p-value
		Lower	Upper	
Sex	1.225	0.776	1.794	0.421
Age	1.034	0.945	1.077	0.335
BMI	0.932	0.745	1.127	0.231
Diabetes	1.381	0.873	2.375	0.179
Hypertension	1.092	0.644	1.684	0.649
Hyperlipidemia	1.173	0.827	1.739	0.201
Smoking	1.124	0.834	1.644	0.346
H/o CAD	1.633	1.121	2.217	<0.001*
Cocaine	1.378	1.106	1.724	0.001*
LVEF	0.877	0.694	1.153	0.113
PASP	1.154	0.878	1.672	0.232
SA	1.024	0.679	1.516	0.863
Viral load	1.412	0.946	2.224	0.422
CD4 count	0.971	0.871	0.995	0.004*
ART duration	0.883	0.819	1.057	0.641
Beta blocker	0.656	0.478	0.902	0.007*
ACE I/ARB	0.570	0.332	1.018	0.098
Spirolactone	1.102	0.876	1.422	0.544
Furosemide	0.724	0.466	1.254	0.328
Antiarrhythmics	0.898	0.644	1.312	0.452
QRS duration	1.536	1.088	2.424	<0.001*

QTc duration	1.125	0.833	1.567	0.243
Higher NYHA class	1.832	1.142	2.938	<0.001*
Appropriate ICD discharge	2.422	1.236	4.028	<0.001*

*p<0.05

† BMI= Body mass index, H/o CAD= History of coronary artery disease, LVEF= left ventricular ejection fraction, PASP= pulmonary artery systolic pressure, SA= sleep apnea, ART= antiretroviral therapy, ACE= angiotensin converting enzyme inhibitors, ARB=angiotensin receptor blocker.

Table S2. Multivariate analysis: Predictors of CV mortality among PHIV with an ICD.

CV mortality outcome	Hazard ratio	95% CI		<i>p</i> -value
		Lower	Upper	
H/o CAD	1.532	1.017	2.531	0.007
Cocaine use	1.344	1.082	1.988	0.004
CD4 count	0.943	0.871	1.193	0.097
Beta Blockers	0.641	0.335	0.861	0.037
QRS duration	1.211	1.033	1.507	0.010
Higher NYHA class	1.376	1.068	1.774	0.002
Appropriate ICD discharge	1.763	1.137	2.631	<0.001

Exact logistic regression for multivariate analysis for ICD discharge. This model included all the covariates with $p < 0.05$ on univariate analysis (Table 3).

Table S3. Comparison of CV outcomes—PHIV vs. non-HIV.

	PHIV (N=59)	Non-HIV (N=267)
CV mortality		
No ICD discharge (n=21 vs. 158)	7 (33%)	34 (22%)
Appropriate / inappropriate ICD discharge (n=23 vs. 53)	17 (74%)	31 (58%)
Appropriate ICD discharge (n=13 vs. 29)	12 (92%)	23 (79%)
Inappropriate ICD discharge (n=10 vs. 24)	5 (50%)	8 (33%)
ATP (n=15 vs. 56)	6 (40%)	14 (25%)
30-day HF readmission		
No ICD discharge (n=21 vs. 158)	11 (52%)	61 (39%)
Appropriate / inappropriate ICD discharge (n=23 vs. 53)	19 (83%)	36 (68%)
Appropriate ICD discharge (n=13 vs. 29)	13 (100%)	25 (85%)
Inappropriate ICD discharge (n=10 vs. 24)	6 (60%)	11 (46%)
ATP (n=15 vs. 56)	8 (53%)	24 (42%)

*p-value >0.05 for all PHIV vs. non-HIV comparisons.

Table S4. ICD therapy and outcomes comparison PHIV on ART vs PHIV not on ART.

	PHIV on ART (N=48)	PHIV not on ART (N=11)	<i>p</i>-value
ICD therapy			0.380
ICD discharge	18 (37.5%)	5 (45%)	
ATP	11 (23%)	4 (36%)	
Type of ICD discharge			0.315
Appropriate ICD discharge	9 (19%)	4 (36%)	
Inappropriate ICD discharge	9 (19%)	1 (9%)	
CV mortality among PHIV with ICD discharge	(N=18)	(N=5)	
	13 (72%)	4 (80%)	0.826
30-day HF readmission among PHIV with ICD discharge			
	14 (78%)	5 (100%)	0.539