

Burden of Arrhythmia in Hospitalized HIV Patients

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Abstract

Background: The improved life expectancy observed in patients living with Human Immunodeficiency Virus (HIV) infection has made age-related cardiovascular complications, including arrhythmias, a growing health concern. We describe the temporal trends in frequency of various arrhythmias and assess impact of arrhythmias on hospitalized HIV patients using the Nationwide Inpatient Sample (NIS) Methods and Results: Data on HIV-related hospitalizations from 2005 to 2014 were obtained from the NIS using International Classification of Diseases, 9th Revision (ICD-9) codes. Data was further subclassified into hospitalizations with associated arrhythmias and those without arrhythmia. Baseline demographics and comorbidities were determined. Outcomes including in-hospital mortality, cost of care, and length of stay were extracted. SAS 9.4 (SAS Institute Inc., Cary, North Carolina) was utilized for analysis. A multivariable analysis was performed to identify predictors of arrhythmias among hospitalized HIV patients. Among 2,370,751 HIV-related hospitalizations identified, the overall frequency of any arrhythmia was 3.01%. Atrial fibrillation (AF) was the most frequent arrhythmia (2110 per 100,000). The overall frequency of arrhythmias has increased over time by 108%, primarily due to a 132% increase in AF. Arrhythmias are more frequent among older males, lowest income quartile and non-elective admissions. Patients with arrhythmias had a higher in-hospital mortality rate (9.6%). In-hospital mortality among patients with arrhythmias has decreased over time by 43.8%. The cost of care and length of stay associated with arrhythmia-related hospitalizations were mostly unchanged. **Conclusions:** Arrhythmias are associated with significant morbidity and mortality in hospitalized HIV patients. AF is the most frequent arrhythmia in hospitalized HIV patients.

Clinical Perspectives

What is New?

- Using a large database, we showed that cardiac arrhythmias among hospitalized HIV patients are associated with increased morbidity and mortality
- Atrial fibrillation is the most frequent arrhythmia among hospitalized HIV patients
- Arrhythmias tend to be more frequent in. older males, lowest. Income. Quartile and non-elective admissions.
- Overall, the in-hospital mortality among hospitalized HIV patients with arrhythmias has decreased over time.

What are the clinical implications?

These findings warrant an aggressive screening and treatment strategy for arrhythmias in the HIV population. Older males and those with lower incomes warrant special attention. A collaboration between infectious

disease specialists and cardiologists would be useful for stratification of cardiovascular risk and mitigating cardiac arrhythmias.

INTRODUCTION

According to the Center for Disease Control and Prevention (CDC), there were 39,782 incident cases of human immunodeficiency virus (HIV) infection in 2016 in the United States¹. The incidence of newly diagnosed HIV infection has been relatively stable over the years since the late 1990s². Access to effective antiretroviral therapy (ART) has substantially reduced HIV mortality, acquired immune deficiency syndrome (AIDS) and AIDS-related hospitalizations. This has led to an overall improved life expectancy in the HIV patient population³. However, in the aging HIV-infected population, cardiovascular complications such as hypertension, coronary artery disease (CAD) and congestive heart failure (CHF) have become a growing health concern⁴⁻⁷. Besides advancing age, other contributors such as the HIV infection itself, immune dysfunction, chronic inflammation, ART exposure and toxicity are also implicated in heart disease and can lead to complications such as myocardial infarction and cardiomyopathy^{8, 9}. In addition to these cardiovascular complications, arrhythmias have also become important contributors to cardiovascular morbidity and mortality in patients with HIV^{10, 11}. However, temporal trends of the frequency and outcome of arrhythmias in patients with HIV have not been adequately described.

We sought to describe the temporal trends in the frequency of arrhythmias among hospitalized HIV patients. We also aimed to identify comorbidities associated with arrhythmias in this specific patient population. In addition, we sought to determine the outcomes related to arrhythmias in hospitalized HIV patients, including in-hospital mortality, length of stay and cost of care.

METHODS

Data Source

The data were obtained from the Nationwide Inpatient Sample (NIS) data set from 2005 to 2014¹². The NIS is a nationally representative survey of hospitalizations conducted by the Healthcare Cost and Utilization Project in collaboration with the participating states. It is the largest all-payer inpatient data set in the United States and includes a sample of US community hospitals that approximates 20% of all US community hospitals¹³. Each entry contains information on demographic details, including age, sex, insurance status, primary and secondary procedures, hospitalization outcome, total cost, and length of stay. The NIS database contains clinical and resource use information, with safeguards to protect the privacy of patients, physicians, and hospitals. The NIS database results have been shown to correlate well with other hospitalization discharge databases in the United States¹³. It has also been used to explain trends in other acute medical and surgical conditions¹⁴.

Study Population

Our target population consisted of HIV-related hospitalizations from January 1, 2005 to December 31, 2014. We included hospital admissions with a diagnosis of HIV infection (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] code 042 and V08) in primary and secondary diagnostic field during our study period. We excluded patients with missing information about sex, mortality, age and age less than 18 years. Since NIS represents a 20% stratified random sample of US hospitals, analyses were performed using hospital-level discharge weights provided by the NIS to obtain national estimates. Our final population of HIV patients. We subclassified this group into hospitalizations with associated cardiac arrhythmia and those without arrhythmia for trend analysis using ICD codes for cardiac arrhythmias such as ventricular tachycardia (VT), ventricular fibrillation (VF)/flutter, supraventricular tachycardia (SVT), AF and, atrial flutter(AFL) listed in Supplementary table 1. Interventions such as ICD implantation, use of vasopressors, cardiac catheterization, endotracheal intubation and CPR were identified by ICD codes in both primary and secondary procedural field (Supplementary Table 1).

Definition of Variables

We used NIS variables to identify patient age, sex, and other patient level variables, such as admission type (elective vs. non-elective), admission day (weekend vs. weekdays); hospital level variables, such as hospital bed size (small vs. medium vs. large), hospital teaching status (non-teaching vs. teaching), and hospital region (Northeast vs. Midwest vs. South vs. West). We divided age into 4 subgroups: 18 to 49 years of age, 50 to 64 years of age, 65 to 79 years of age, and 80 years of age and older. We defined the severity of comorbid conditions by using the Deyo modification of the Charlson Comorbidity Index. This index contains 17 comorbid conditions with differential weights. The score ranges from 0 to 33, with higher scores corresponding to greater burden of comorbid diseases. Facilities were considered to be a teaching hospital if they had an American Medical Association–approved residency program, were a member of the Council of Teaching Hospitals, or had a full-time equivalent interns and residents to patient’s ratio of 0.25 or higher¹⁵. The bed size cutoff points divided into small, medium, and large have been done so that approximately one-third of the hospitals in each region, location, and teaching status combination would fall within each bed size category¹⁶. Co-morbidities associated with hospitalization for HIV infection were identified using AHRQ comorbidity measures, i.e., by using ICD-9-CM diagnoses and the Diagnosis Related Group (DRG) in effect on the discharge date¹⁷.

In hospital mortality, Cost and Length of stay

In-hospital mortality was defined as death from any cause during the same hospital stay. LOS was already provided by the Healthcare Cost and Utilization Project (HCUP) for each entry. Disposition to another facility included transfer to skilled nursing facility, intermediate care facility, and nursing homes. The HCUP NIS contains data on total charges for each hospital in the databases, which represents the amount that hospitals billed for services. To calculate estimated cost of hospitalizations, the NIS data were merged with Cost to Charge Ratios (CCR) available from HCUP^{18, 19}. Using the merged data elements from the CCR files and the total charges reported in the NIS database, we converted the hospital total charge data to cost estimates by simply multiplying total charges with the appropriate CCR. These costs are essentially standardized, can be measured across hospitals, and are used for the remainder of this report. Adjusted annual costs were calculated in terms of the 2013 cost, after adjusting for inflation according to the latest consumer price index data released by the US government on February 15, 2017²⁰.

Statistical Analysis

The statistical software package SAS 9.4 (SAS Institute Inc., Cary, North Carolina) was utilized for the analyses, which accounted for the complex survey design and clustering. Since NIS represents a 20% stratified random sample of US hospitals, analyses were performed using hospital-level discharge weights provided by the NIS to obtain national estimates of arrhythmia associated with HIV hospitalizations. For categorical variables such as annual change in HIV hospitalization rate and in-hospital mortality, the modified chi-squared test of trend for proportions (Cochrane Armitage test) was used²¹. For continuous variable such as LOS and cost of care, simple linear regression was used. Multivariable models for predictors of arrhythmia were performed with independent variables which were either clinically significant or statistically significant in univariate model. Multivariate model included patient-level variables such as age and gender; year of admission, admission type (elective vs non-elective), day of admission (weekdays vs weekend), primary payer (private insurance [including Health Maintenance Organization] and self-pay versus Medicaid/Medicare); co-morbidities such as diabetes mellitus, chronic lung disease, peripheral vascular disease etc.; hospital course requiring ICD implantation, use of vasopressors, cardiac catheterization, endotracheal intubation and CPR; A two-sided p-value < 0.05 was considered statistically significant.

RESULTS

We identified 2,370,751 HIV-related hospitalizations from January 1, 2005 through December 31, 2014. The frequency of all variables is per 100,000 hospitalizations, unless specifically mentioned.

Frequency of Arrhythmias:

Among 2,370,751 HIV-related hospitalizations, 71,285 hospitalizations had either a primary or secondary

arrhythmia-related diagnosis. This amounts to a 3.01% frequency of arrhythmia-related diagnoses in HIV related hospitalization (Table 1). The frequency of specific arrhythmias (per 100,000 hospitalizations) in the study was as follows: 2110 AF, 560 VT, 420 AFL, 170 SVT and 130 VF.

From 2005 through 2014, the frequency of arrhythmia among HIV-related hospitalizations has increased by 108% (from 4412 in 2005 to 9435 in 2014). This increase in arrhythmia was primarily the result of the increased frequency of AF (132.5% increase, from 2898 patients in 2005 to 6955 in 2014), followed by VT (72.1 % increase, from 985 in 2005 to 1735 in 2014) and AFL (192.7% increase, from 427 in 2005 to 1265 in 2014). The frequency of SVT has remained relatively stable over the years (14.8% increase), as shown in Figure 1 ($P < 0.001$ for all trends).

Demographics:

Baseline characteristics of HIV-related hospitalizations with arrhythmias are summarized in Table 2. Arrhythmias were most commonly present in patients aged 50-64 (49.3%). This is in contrast to the predominantly younger age group found in all hospitalizations. 61.2% of hospitalized HIV patients were in the 18-49 age range, and the 50-64 age group comprised 33.9% of all hospitalizations. While there was an increase in frequency of arrhythmias in all age groups, the increase in frequency was greatest in patients aged 18-49 (81% relative increase). Figure 2 illustrates the temporal trends in frequency of any arrhythmia per 100,000 HIV hospitalizations within various age groups.

The majority of arrhythmias were present in males (76.42%) compared to females (23.58%). Over the years, there was a comparable increase in the frequency of arrhythmias among both genders (138% in males and 147% in females). Arrhythmias were most frequent in patients within lowest quartile for household income (0-25th percentile, 44.85%). Arrhythmias were less frequent with every increase in quartile for household income. Similar to all HIV hospitalizations, patients with arrhythmias were most commonly admitted non-electively (90.77%) and on weekdays rather than weekends (78.14% versus 21.86%). Most of these patients had Medicare as their primary payer (74.72%). The majority of them were admitted to teaching hospitals (69.25%). Patients with arrhythmia had a greater burden of comorbidities, as evidenced by a Deyo/Charlson score of [?]2, which was present in 81.64% of patients with any arrhythmia, compared to 72.42% found in patients with no arrhythmias ($P < 0.0001$).

Among all comorbidities assessed, patients with any arrhythmia had a significantly greater frequency of hypertension (55.56% versus 33.94%), congestive heart failure (31.73% versus 6.03%), renal failure (29.06% versus 12.9%), chronic pulmonary disease (26.23% versus 19.16%), CAD (24.31% versus 6.54%), diabetes mellitus (23.43% versus 13.8%), hyperlipidemia (22.22% versus 10.16%), previous myocardial infarction (8.24% versus 2.37%), previous CABG (4.23% versus 0.94%) and obesity (6.98% versus 3.86%) compared to hospitalized patients with no arrhythmias ($P < 0.0001$ for all comorbidities) (Figure 3).

Hospital course in Patients with any Arrhythmia

Hospitalization course among patients with arrhythmias is summarized in Table 2. HIV-related hospitalizations with arrhythmias had a statistically significant longer average length of stay, compared to without arrhythmias (5 days vs 4 days; $P < 0.0001$). The median cost of care was significantly higher in patients with arrhythmias compared to all hospitalizations (\$12210 versus \$7665, IQR \$6248-\$26167 in patients with arrhythmias and \$4435-\$14336 in all hospitalizations; $P < 0.0001$). The median length of stay and cost of care in HIV-related hospitalizations with arrhythmias has mostly remained unchanged over the years (P value of 0.0483 and 0.4019 respectively).

Markers of increased disease severity were more common among HIV-related hospitalizations with arrhythmia compared to patients with no arrhythmia. These include vasopressor use (1.3% versus 0.24%), cardiac catheterization (7.17% versus 1.54%), cardiac arrests (4.09% versus 0.42%), CPR (3.4% versus 0.41%) and endotracheal intubation (12.75% versus 3.7%).

All-cause in-hospital mortality was associated with the presence of any cardiac arrhythmia. Patients with arrhythmias had an in-hospital mortality rate of 9.6%, as opposed to a rate 2.84% found in patients with no

arrhythmia. However, the in-hospital mortality rate in patients with any arrhythmia has decreased over the years from 12.35% in 2005 to 7.9% in 2014 (decrease of 43.8%; $P < 0.001$ for trend). Among the arrhythmias, the highest reduction in in-hospital mortality was observed in patients with VT (decrease of 57.5%; $P < 0.0001$ for trend).

As anticipated, the highest in-hospital mortality was associated with patients who had VF (46.11%), followed by VT (14.48%), SVT (8.73%) and atrial flutter (7.51%). Despite being the most frequent arrhythmia in HIV patients, AF was associated with the numerically lowest in-hospital mortality (6.8%). Results for in-hospital mortality throughout the years, stratified by arrhythmia type are summarized in Table 3.

Association of Arrhythmias in HIV Patients with Demographics and Comorbidities:

On multivariate analysis, later year of admission had a higher odds ratio (OR) for arrhythmia among HIV patients compared to earlier years (year 2014 vs 2005 OR was 1.391; $P < 0.0001$). Older age was also associated with arrhythmias (OR 1.055; $P < 0.0001$). Female sex was associated with lower odds of arrhythmias (OR 0.689, $P < 0.0001$).

Among comorbidities assessed, congestive heart failure had the strongest correlation with arrhythmias (OR 3.345; $P < 0.0001$), followed by obesity (OR 1.504; $P < 0.0001$), coronary artery disease (OR 1.46; $P < 0.0001$), renal failure (OR 1.397; $P < 0.0001$), hypertension (OR 1.205; $P < 0.0001$) and chronic pulmonary disease (OR 1.183; $P < 0.0001$).

In addition, cardiogenic shock, cardiac arrest and endotracheal intubation had high OR for arrhythmias (OR 3.18, 2.966 and 2.261 respectively; $P < 0.0001$ for all).

Higher income was associated with arrhythmia-related hospitalization in HIV patients (OR 1.279 in patients with top quartile for income; $P < 0.0001$). Other variables assessed, including type of admission (elective vs. non-elective), day of admission (weekend vs. weekday) and hospital bed size were not strongly associated with arrhythmias. The multivariate predictors of arrhythmias are listed in Table 4.

DISCUSSION

In this analysis of HIV-related hospitalizations from 2005 through 2014, we report an increase in the frequency of arrhythmias over time. The presence of arrhythmia is associated with adverse outcomes, including a higher rate of in-hospital mortality. In the current study, we report a 108% overall increase in the frequency of arrhythmia among HIV patients during the study period. To the best of our knowledge, this is the first study describing the temporal trends of arrhythmias in hospitalized HIV patients over time. Variables independently associated with the presence of arrhythmia in HIV-related hospitalizations include male sex, older age, higher income, later year of admission and the presence of comorbidities such as congestive heart failure, obesity, coronary artery disease (CAD), renal failure, hypertension, chronic pulmonary disease, history of previous myocardial infarction and peripheral vascular disease. It is notable that the frequency of these comorbidities has also increased over time, which could be contributing to the rise in overall frequency of arrhythmias during the study period. Although the association between all-cause in-hospital mortality and arrhythmia was significant, the mortality rate among patients with any arrhythmia declined over the time. The contributory factors to this decrease are unclear, but could relate to improved diagnosis and management of cardiovascular disease. This trend was consistent with the decrement in all-cause mortality found in HIV patients in general, as reported by multiple studies worldwide²²⁻²⁴.

In our analysis, AF has emerged as the most frequent arrhythmia among hospitalized HIV patients. Our reported frequency of AF was 2.11%. This is concordant with a previous analysis of the Veterans Affairs HIV Clinical Case Registry, which reported a frequency of 2.6% of atrial fibrillation in a large cohort of over 30,000 HIV patients from 1996 to 2011¹⁰.

While our study does not address the mechanisms underlying the significant frequency of arrhythmias in the setting of HIV, other studies may provide insight. HIV infection is known to be an important risk factor for atherosclerosis and stroke^{25, 26}, and similar mechanisms can explain the incidence of arrhythmias

in that population. Both advanced age and inflammation have been associated with an increased risk for developing arrhythmias such as AF^{27, 28}, making older patients with chronic HIV particularly susceptible to developing it. Indeed, persistent immunodeficiency, accelerated immunosenescence and inflammation in HIV patients were found to accelerate the onset of age-associated diseases, including cardiovascular diseases and arrhythmias such as AF²⁹. Elution of inflammatory cytokines and reactive oxygen species by infected cardiac endothelium; expression of HIV-associated proteins that lead to destruction of mitochondria and myocardial damage, are mechanisms previously implicated in the pathogenesis of AF in HIV infected patients³⁰. The severity of the HIV infection also correlates with the risk of developing AF. A previous analysis identified low CD4+ cell count and high HIV RNA viral load as independent variables for the development of AF in HIV patients¹⁰. However, the exact mechanism underlying this correlation is difficult to establish given that many patients in the HIV population share similar risk factors for AF, such as hypertension, CAD and heart failure, as evidenced by our study. Additionally, components of highly active antiretroviral therapy (HAART) such as protease inhibitors are associated with development of metabolic syndrome, which is a risk factor for AF³¹.

In our study, the frequency of malignant arrhythmias such as VF and VT has increased over the years. While the reason behind this rise is unclear, previous studies showed that patients with HIV can have a prolonged QTc, predisposing them to malignant arrhythmias including torsades de pointes, sustained VT and VF. This prolongation can be a direct result of the HIV infection itself, and can be observed in the absence of overt cardiovascular disease^{7, 32}. The severity of the HIV infection, evidenced by a low CD4+ cell count and high viral load, has been shown to be a risk factor for the development sudden cardiac death (SCD)¹¹. Furthermore, medications frequently administered to HIV patients, including pentamidine, TMP-SMX (Trimethoprim-Sulfamethoxazole), non-nucleoside reverse transcriptase inhibitor efavirenz (Sustiva), and protease inhibitors such as atazanavir (Reyataz)³³, have also been associated with QTc prolongation^{7, 34, 35}. It is possible that the increasingly widespread use of such medications contributed to the rise of malignant arrhythmias in the HIV population over the study years. Furthermore, the increased frequency of cardiovascular conditions such as CAD and CHF in the HIV population, as shown by our study, have likely contributed to the rise of such arrhythmias. These findings call for increased scrutiny to the QTc interval in HIV patients, and warrant considering HIV disease status in the risk assessment of malignant arrhythmias.

STUDY LIMITATIONS

Our study has a number of limitations which need to be addressed. Firstly, there are constraints with using administrative claims data such as the NIS³⁶. It is a de-identified database; making it impossible to validate individual ICD-9 codes. Therefore, inaccuracies in coding may occur. Furthermore, electrograms and telemetry strips were not available to validate the type of arrhythmia in our sample. We were unable to subcategorize the type of arrhythmia in our sample, such as identifying persistent versus paroxysmal AF. In addition, the NIS does not provide long term follow-up data. Therefore, it is probable that outcomes were underestimated in our study. The NIS regards each hospitalization as a separate entity, so it is possible that readmissions were regarded as distinct hospitalizations, leading to an overestimation in the number of hospitalizations. The cause of in-hospital mortality could not be ascertained since hospitalization notes are unavailable through the NIS. It is uncertain whether changes in coding practice patterns contribute to the changes in reported arrhythmia frequency, using NIS methodology.

Apart from the aforementioned limitations, it is also possible that patients with arrhythmias had comorbid conditions that we have not assessed. Therefore, we cannot completely exclude the possibility that additional unknown confounding variables, not included in our multivariate analysis, may explain some of the associations found. We could not, for instance, ascertain the extent at which concurrent medication use such as anti-retroviral therapy (ART) impacted the incidence of arrhythmias, nor could we determine the relationship between disease severity (CD4 count or viral load, for instance) and arrhythmia risk. Future studies should be aimed at investigating the various drug regimens for HIV and their associated risk of developing arrhythmias. Data on CD4+ cell count and HIV viral load was not collected in our sample as they were not available in the NIS registry. Further studies are warranted to elucidate the specific mechanisms

by which HIV can lead to the development of AF. Lastly, our sample did not include uninfected controls to allow a direct comparison of the burden of arrhythmias between HIV and non-HIV patients. Such a study is warranted to determine if HIV infection is an independent risk factor for the development of arrhythmias. Unfortunately, it was not possible to perform this analysis using the NIS registry, given the very large population of uninfected controls that would have to be included in the analysis (approximately 80 million patients from the years 2005-2014).

These limitations are, however, counterbalanced by the presence of a large unrestricted study sample which lacks the selection bias found in studies reported by individual specialized centers and skilled operators.

CONCLUSION

Among hospitalized HIV patients, cardiac arrhythmias are associated with significant patient morbidity and mortality. AF has emerged as the most frequent arrhythmia among hospitalized HIV patients. The presence of arrhythmias is associated with adverse outcomes in HIV patients, including a higher in-hospital mortality rate and cost of care. The in-hospital mortality among patients with any arrhythmia is significant but has decreased over the years.

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FIGURES AND TABLES

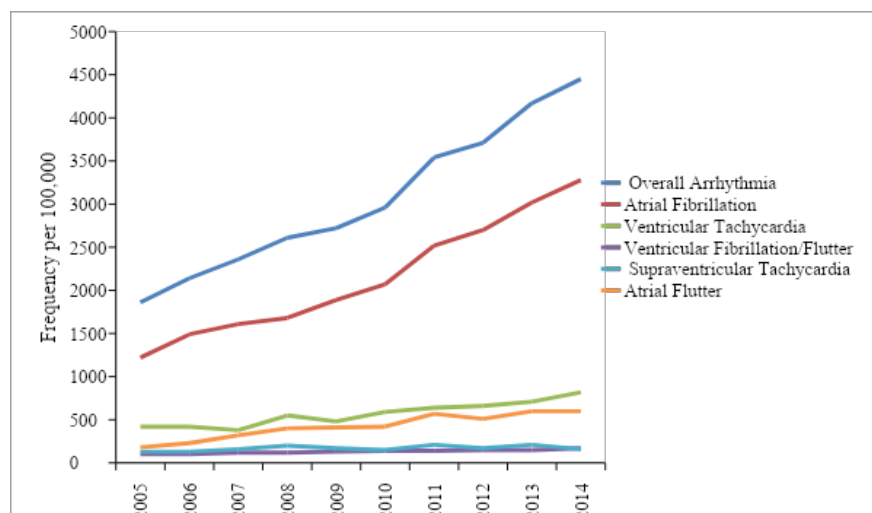


Figure 1. Frequency of arrhythmia-related hospitalizations by arrhythmia type for the entire study period.

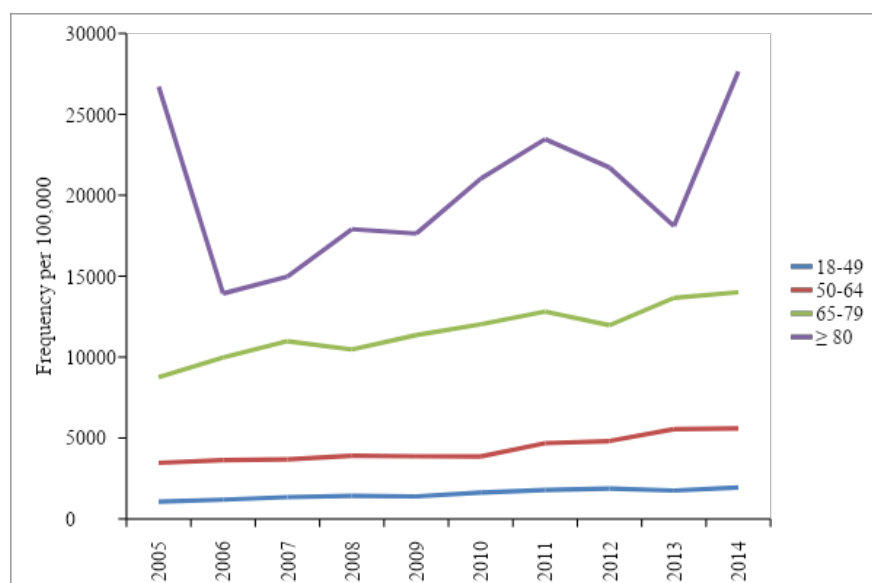


Figure 2. Temporal trends in frequency of any arrhythmia per 100,000 HIV hospitalizations within various age groups.

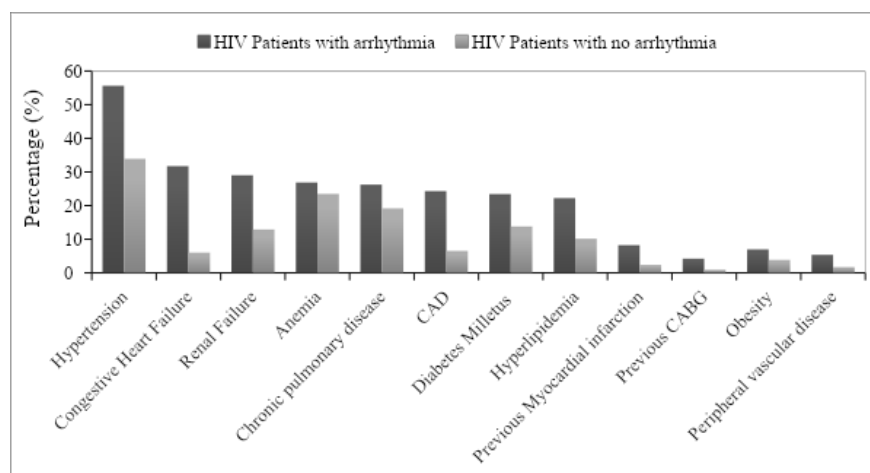


Figure 3. Percentage of comorbidities among HIV patients with arrhythmia and with no arrhythmia. CAD: Coronary Artery Disease, CABG: Coronary Artery Bypass Graft.

	Patients with Arrhythmia	Patients without Arrhythmia
Primary admission	71285 (3.01%)	2299466
Patient level variables		
Age		
18-49	30.42	62.2
50-64	49.25	33.38
65-79	18.47	4.21
80	1.87	0.22
Gender		
Male	76.42	65.73
Female	23.58	34.27
Deyo/Charlson Score		
<2	18.36	27.58
>=2	81.64	72.42
Hospital course		
Use of Vasopressor	1.3	0.24
Cardiac Catheterization	7.17	1.54
Endotracheal Intubation	12.74	3.7
CPR	3.4	0.41
Cardiogenic shock	1.9	0.12
Cardiac Arrest	4.09	0.42
Median household income category for patient's zip code		
1. 0-25th percentile	44.85	49.39
2. 26-50th percentile	22.9	23.05
3. 51-75th percentile	19.16	17.03
4. 76-100th percentile	13.09	10.54
Primary Payer		
Medicare / Medicaid	74.72	70.13
Private including HMO	17.36	15.7
Self-pay/no charge/other	7.8	13.95
Missing	0.12	0.22
Admission type		

Non-elective	90.77	88.28
Elective	9.23	11.72
Admission day		
Weekdays	78.14	78.85
Weekend	21.86	21.15
Hospital characteristics		
Hospital bed size		
Small	8.64	9.38
Medium	24.47	24.3
Large	66.89	66.32
Hospital teaching status		
Non-teaching	30.75	29.33
Teaching	69.25	70.67
Discharge		
Home	68.33	78.78
Facility	19.04	12.76
In hospital Mortality	9.6	2.84
Length of Stay during index admission in days (Median, IQR)	5(3-10)	4 (2-7)
Cost of care (Median, IQR)	12210 (6248-26167)	7577 (4401-14083)

Table 1. Comparison of baseline characteristics and course of hospitalization between HIV patients with arrhythmias and without arrhythmias from 2005 through 2014. Abbreviations: CPR: cardiopulmonary resuscitation, HMO: Health Maintenance Organization, IQR: Interquartile Range.

	2005	2006	2007
Primary admission	4412	5629	5709
Patient level variables			
Age			
18-49	1060	1190	1350
50-64	3460	3640	3680
65-79	8750	9980	10980
80	26710	13930	14970
Gender			
Male	2120	2530	2730
Female	1310	1400	1690
Deyo/Charlson Score			
<2	1380	1620	1550
>=2	2040	2330	2650
Comorbidities			
Hyperlipidemia	3540	4350	4430
History of hypertension	2960	3510	3850
Diabetes Miletus	2530	3770	3920
Chronic pulmonary disease	2400	3030	3220
Peripheral vascular disease	5230	5010	7930
Neurological disorder or paralysis	1970	2410	2160
Hematological or oncological malignancy	2520	2300	3320
Anemia	1690	1990	2330
Obesity	3080	3640	4700
Coronary artery disease	7390	8120	8300
History of Previous Myocardial infarction	7050	5930	8140
History of Previous CABG	9200	6720	6970

Congestive Heart Failure	9850	10530	13190
Renal Failure	4570	4690	5090
Hospital course			
Use of Vasopressor	10640	9320	12270
Cardiac Catheterization	9310	10480	11400
Endotracheal Intubation	6840	6910	8780
CPR	14460	14360	19390
Cardiogenic shock	28090	22160	25100
Cardiac Arrest	14020	15370	18960
Median household income category for patient's zip code			
1. 0-25th percentile	1840	2080	2170
2. 26-50th percentile	1740	2290	2360
3. 51-75th percentile	1890	2160	2540
4. 76-100th percentile	2350	2540	3130
Primary Payer			
Medicare / Medicaid	1900	2280	2550
Private including HMO	2390	2190	2750
Self-pay/no charge/other	1020	1460	1290
Admission type			
Non-elective	1910	2250	2460
Elective	1550	1310	1630
Admission day			
Weekdays	1810	2120	2350
Weekend	2070	2210	2420
Hospital characteristics			
Hospital bed size			
Small	2110	1910	1900
Medium	1330	2000	2470
Large	2040	2230	2370
Hospital teaching status			
Non-teaching	2000	2300	2580
Teaching	1780	2080	2240
Discharge			
Home	1670	1890	2040
Facility	2350	2990	2930
Length of Stay during index admission in days (Median, IQR)	6 (3-11)	6 (3-11)	5 (3-10)
Cost of care (Median, IQR)	12285 (6446-27184)	12974 (6502-27557)	12181 (6117-27557)

Table 2. Baseline characteristics and course of hospitalization among hospitalized HIV patients from 2005 through 2014. Abbreviations: CABG: Coronary Artery Bypass Graft, ICD: Implantable Cardioverter Defibrillator, CPR: cardiopulmonary resuscitation, HMO: Health Maintenance Organization, IQR: Interquartile Range

(%)	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	Overall
Overall Arrhythmia	12.35	11.21	12.97	10.7	10.21	10.31	9.19	7.48	7.32	7.9	9.6
Ventricular Tachycardia	13.32	16.11	18.56	22.2	18.32	17.09	12.67	8.83	9.93	11.24	14.48
Ventricular Fibrillation/Flutter	56.58	50.89	57.93	49.57	47.67	46.64	42.28	39.39	42.19	34.72	46.11
Supraventricular Tachycardia	9.77	4.22	7.68	10.38	10.42	9.33	11.64	9.72	5.49	7.58	8.73
Atrial Fibrillation	9.71	9.19	9.95	5.67	6.7	7.01	6.85	5.52	5.13	5.61	6.8
Atrial Flutter	12.79	4.51	9.56	8.43	7.18	6.02	7.84	4.07	7.48	9.49	7.51

Table 3. In-hospital mortality in hospitalized HIV patients from 2005 through 2014, stratified by arrhythmia type. Values are presented as percentages (%).

Variables	OR	LL	UL	P-value
Year 2014 vs 2005	1.391	1.271	1.521	<.0001
AGE	1.055	1.053	1.057	<.0001
FEMALE	0.689	0.658	0.721	<.0001
Comorbidities				
Hyperlipidemia	1.116	1.06	1.175	<.0001
History of hypertension	1.205	1.155	1.257	<.0001
Diabetes Miletus	0.936	0.889	0.985	0.0116
Chronic pulmonary disease	1.183	1.132	1.238	<.0001
Peripheral vascular disease	1.133	1.035	1.239	0.0069
Neurological disorder or paralysis	0.988	0.928	1.053	0.718
Hematological or oncological malignancy	1.088	1.006	1.177	0.0339
Anemia	0.964	0.922	1.007	0.0963
Obesity	1.504	1.391	1.627	<.0001
Coronary artery disease	1.46	1.375	1.549	<.0001
History of Previous Myocardial infarction	1.178	1.087	1.276	<.0001
History of Previous CABG	1.099	0.985	1.225	0.0909
Congestive Heart Failure	3.345	3.192	3.505	<.0001
Renal Failure	1.397	1.331	1.465	<.0001
Hospital course				
Use of Vasopressor	1.817	1.503	2.196	<.0001
Cardiac Catheterization	1.748	1.602	1.907	<.0001
Endotracheal Intubation	2.261	2.11	2.424	<.0001
CPR	1.916	1.642	2.234	<.0001
Cardiogenic shock	3.18	2.63	3.847	<.0001
Cardiac Arrest	2.966	2.573	3.42	<.0001
Median household income category for patient's zip code				
0-25th percentile	Referent	Referent	Referent	
26-50th percentile	1.111	1.058	1.166	0.0499
51-75th percentile	1.233	1.171	1.299	0.0002
76-100th percentile	1.279	1.203	1.359	<.0001
Primary Payer				
Medicare / Medicaid	Referent	Referent	Referent	
Private including HMO	1.201	1.141	1.264	<.0001
Self pay/no charge/other	0.843	0.786	0.905	<.0001
Elective vs Non elective	0.808	0.757	0.862	<.0001
weekdays vs weekend	1.016	0.971	1.064	0.4938
Hospital bed size				
Small	Referent	Referent	Referent	
Medium	1.115	1.038	1.198	0.0261
Large	1.111	1.04	1.186	0.021
Teaching vs Non Teaching	0.971	0.932	1.011	0.1489

Table 4. Multivariate Predictors of arrhythmias in hospitalized HIV patients. Abbreviations: CABG: Coronary Artery Bypass Graft, CPR: cardiopulmonary resuscitation, HMO: Health Maintenance Organization.

ICD 9 codes

HIV infection	V08, 042
Cardiac Arrhythmia	
Ventricular tachycardia	427.1
Ventricular fibrillation	427.41
Ventricular flutter	427.42
Atrial fibrillation	427.31
Atrial flutter	427.32
Supraventricular tachycardia	427
In hospital course	
Use of vasopressors	0.17
Cardiac catheterization	88.55, 88.56, 88.57, 37.22, 37.23
Endotracheal intubation	96.04
CPR	99.6
Cardiac arrest	99.60,99.63,427.5
Cardiogenic shock	785.51
Maze procedure	37.33
Ischemic stroke	434, 436
Hemorrhagic stroke	430 ,431
Direct current cardioversion	99.61
Co-morbidities*	
Hyperlipidemia	272
Coronary artery disease	414.00-414.07
History of Previous Myocardial infarction	412
History of Previous CABG	V45.81
Congestive Heart Failure	402.01,402.11,402.91,4.04.01,404.03,404.11,404.13,404.91,404.93,428

Supplementary Table 1: ICD-9 codes used to identify comorbidities and in hospital course related to HIV patients' admission. * Rest of the comorbidities were identified using "CM_" variables provided by HCUP for NIS database.