International Journal of Cardiology xxx (xxxx) xxx



Contents lists available at ScienceDirect

International Journal of Cardiology



journal homepage: www.elsevier.com/locate/ijcard

Burden of arrhythmia and electrophysiologic procedures in alcoholic cardiomyopathy hospitalizations

Samian Sulaiman ^{a,*}, Nazdar Yousef^d, Mina M. Mehanni^a, Sakthi Sundararajan^a, Romina Wingert^e, Michael Wingert^f, Asim Mohammed^c, Arshad Jahangir^b

^a Department of General Internal Medicine, Medical College of Wisconsin, Milwaukee, WI, USA

^b Aurora Cardiovascular Services, Aurora Sinai/Aurora St. Luke's Medical Centers, Milwaukee, WI, USA

^c Division of Cardiology, Medical College of Wisconsin, Milwaukee, WI, USA

^d Kalamoon Medical School, Damascus, Syria

^e Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA

^f University of California, Los Angeles, CA, USA

ARTICLE INFO

Article history: Received 3 November 2019 Received in revised form 17 December 2019 Accepted 27 January 2020 Available online xxxx

ABSTRACT

Background: Limited national US data are available regarding the prevalence of and trends in different arrhythmias and the use of electrophysiological procedures in patients with alcoholic cardiomyopathy.

Methods: This was a cross-sectional study that used the Nationwide Inpatient Sample database (2007–2014). Hospitalizations of adults with alcoholic CMP were identified with the ICD-9 code (425.5). CAD and other causes of cardiomyopathy were excluded. Chi-square test, *t*-test, mixed-effect logistic regression and quantile regression were used.

Results: Among 75,430 hospitalizations, 48% had arrhythmias. Individuals with a co-diagnosis of arrhythmia tended to be older (56.9 vs 53.2-year-old) and male (89.5% vs 81.9%). The most prevalent arrhythmias were atrial fibrillation/flutter (31.5%), followed by ventricular tachycardia (7.9%). The prevalence of arrhythmias increased from 44% to 50% (2007–2014) (p < 0.001) and this increase was mainly secondary to the increasing prevalence AFib/AFL Excluding cardiac arrest, arrhythmias were not associated with increased in-hospital mortality. The median length of stay and total charges for arrhythmia vs no-arrhythmia hospitalizations were 5 vs 4 days (p < 0.001) and \$31,127 vs \$24,199 respectively (p < 0.001). EP procedures were performed in 5.6% of all hospitalizations and it increased from 5.2% to 6% (2007–2014) (p = 0.2). The most common procedures were cardioversion (2.7%), ICD placement (2.2%) and PPM placement (1.1%).

Conclusion: Arrhythmias were reported in 48% of hospitalizations. There was an increasing burden of arrhythmias secondary to increasing atrial fibrillation. Excluding cardiac arrest, arrhythmias were not associated with increased in-hospital mortality but were associated with longer hospital stays and higher total charges.

© 2020 Elsevier B.V. All rights reserved.

1. Introduction

Alcohol is a leading cause of non-ischemic dilated cardiomyopathy in developed countries [1]. Alcoholic cardiomyopathy (ACMP) is an acquired form of dilated cardiomyopathy associated with excessive alcohol drinking (>80–90 g per day over >5 years) [2]. The prevalence of ACMP ranges between 23% and 47% among the patients with idiopathic dilated cardiomyopathy [1]. ACMP is associated with atrial and ventricular arrhythmias. However, there is a paucity of national studies in the US examining the burden of arrhythmia and conduction disorders in this population.

 \star All authors above take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

* Corresponding author at: 2062 Pinecrest Dr., Morgantown, WV 26505, USA. *E-mail address:* samian.sulaiman@hsc.wvu.edu (S. Sulaiman).

https://doi.org/10.1016/j.ijcard.2020.01.068 0167-5273/© 2020 Elsevier B.V. All rights reserved. The aim of this study was to identify the burden of and trend in different arrhythmias in the hospital stays of patients with a history of ACMP and evaluate the inpatient utilization of electrophysiological procedures in this population over 8 years (2007–2014).

2. Methods

2.1. Data source

The National Inpatient Sample (NIS) database 2007–2014 was used. This database is the largest publicly available all-payer inpatient database in the US. Details of the design and description of the NIS elements are available online [3]. The NIS includes information on demographics, inpatient diagnoses and procedures, total charges, primary payers, length of stay and hospital characteristics. Because no patient identifiers

<u>ARTICLE IN PRESS</u>

were used, this study was deemed exempt from institutional review board approval.

2.2. Identification of alcoholic cardiomyopathy hospitalizations and burden of arrhythmia

Hospital stays for adults (\geq 18 years) with a primary or secondary diagnosis of ACMP were identified with ICD-9 code (425.5). A primary diagnosis is a condition that is responsible for the admission of patient to the hospital. Secondary diagnoses could be comorbidities present before admission or complications that developed throughout the hospital stay. Because ACMP diagnosis is made through exclusion, all hospital stays with a co-diagnosis of ischemic (history of CAD or MI), hypertensive, valvular or congenital heart disease, or carditis were excluded (see the supplementary material for ICD-9 codes).

Three broad categories of arrhythmias were identified:

- 1- Conduction disorders: included all types of AV blocks and bundlebranch blocks.
- 2- Dysrhythmias: included all types of tachycardia (ventricular and supra-ventricular) in addition to sinoatrial node dysfunction.
- 3- Cardiac arrest: included cardiac arrest, ventricular fibrillation and ventricular flutter.

Cardiac implanted electronic device (CIED) in situ included patients who had a PPM or ICD before admission (identified with ICD-9 diagnosis codes; see the supplementary material). New implantations of CIEDs during current hospitalizations were identified with ICD9 procedure (Not diagnosis) codes and were not included in this category.

2.3. Statistical analysis

Microsoft Excel (2010), STATA 15.1 (StataCorp, College Station, TX) [4] and RStudio version 3.5.1 (The R Foundation for Statistical Computing Platform, Vienna, Austria) [5] were used for statistical analysis, accounting for survey design, sampling weights, primary sampling units and strata (the year was added to NIS strata).

Categorical data were tested with Pearson's chi-square test. Continuous variables were tested with survey linear regression analysis. Because the length of stay and total charges had skewed distributions, medians and quantile regression were used to compare different groups. Trends over the years were tested with linear regression (for continuous variables) and chi-square test for categorical variables. To identify predictors of in-hospital mortality, mixed-effect multivariate logistic regression was used to measure odds ratios and patient-level and hospital-level predictors were included. Standard errors were estimated with Taylor series linearization, all p values were two sided, and type I error was set at 0.05. The Holm-Bonferroni adjustment was used to control type I error at a level <0.05 when multiple comparisons were performed simultaneously such as in multivariate logistic regression. Some data were missing particularly for race (15.1%). The remaining variables were largely complete with only <5% missing.

The US adult population estimates were obtained from the CDC website [6]. Age-adjusted mortality rates were calculated with the 2000 US projected population as the external standard population. The following age categories were used: 18-44, 45-64 and ≥ 65 years of age.

3. Results

3.1. Comparison of demographics, comorbidities and hospital-level characteristics between arrhythmia and non-arrhythmia associated hospitalizations

Among total of 75,430 of ACMP hospital stays, ACMP/CHF was the primary diagnosis in 24% and the secondary diagnosis in 76%. Arrhythmias were reported in 48.2% of all ACMP hospitalizations but were the

primary diagnosis in only 10.6% of hospitalizations (please refer to the Fig. 3 in the supplementary material for the extended list of primary diagnoses).

Individuals in the arrhythmia group were older than those in the non-arrhythmia group (56.9 vs 53.2, p < 0.001) and had a higher proportion of males (89.5% vs 81.9%, p < 0.001) and Caucasians (60.2% vs 50.6%, p < 0.001), but a lower proportion of African-Americans (16.1% vs 23.9%, p < 0.001). The arrhythmia group had a higher proportion of hospitalizations than the non-arrhythmia group in the Northeast and the West, but a lower proportion in the South and Midwest. The arrhythmia group, compared with the non-arrhythmia group, had a greater proportion of patients with higher socio-economic status (3rd and 4th quartile, p < 0.001) and a greater proportion of Medicare patients (35.8% vs 31.6%, p < 0.001) but a lower proportion of Medicaid patients (19.8% vs 25.2%, p < 0.001) (Table 1).

The arrhythmia group had a lower prevalence of the following comorbidities in univariate analysis (all with p < 0.05): CHF, liver disease, and drug abuse. The arrhythmia group had higher prevalence of shock, respiratory failure, CVA and obesity (all with p < 0.05) (Table 1).

3.2. Burden of arrhythmia, yearly trend and predictors of arrhythmia

Cardiac arrhythmias were reported in 48.2% of hospitalizations but were the primary diagnosis in only 10.6% of hospitalizations. Conduction disorders were reported in 5.4% of hospitalizations (primary diagnosis 0.2%, secondary diagnosis 5.2%, and both 0.1%). Dysrhythmias were reported in 44% of hospitalizations (primary diagnosis 6.9%, secondary diagnosis 34.2%, and both 2.9%). Cardiac arrest was reported in 3% of all hospitalizations (primary diagnosis 0.4%, secondary diagnosis 2.3%, and both 0.2%).

The most common arrhythmias were AFib/AFL 31.5%, VT 7.9%, unspecified dysrhythmia 6.4% and BBB 4.1% (Fig. 1). In 2007, arrhythmias were reported in 44% of hospitalizations; this proportion peaked at 52.8% in 2013 and then decreased to 50.2% in 2014 (p < 0.001) (Fig. 1). Statistically significant differences over the years were found for total arrhythmia and AFib/AFL (p < 0.05). The AFib /AFL was reported in 30.1% in 2007, peaked at 34.1% in 2013 and decreased to 32.4% in 2014 (p < 0.01). The cardiac arrest was reported in 3% in 2007 and increased to 4.2%, in 2014 (p = 0.5) (Fig. 1).

To understand the increasing trend in atrial fibrillation prevalence over the years, we conducted multivariate mixed effect logistic regression to identify independent predictors of atrial fibrillation in our cohort. Identified independent predictors were age, male sex, Caucasian race, hypothyroidism, sleep apnea and obesity (supplementary material). Over the same period, there was an increasing trend in obesity and sleep apnea from 2007 to 2014 (see the supplementary material).

The independent predictors of cardiac arrest in multivariate mixedeffect logistic regression were electrolyte disorders, LBBB, Southern & Western US regions, smoking and depression (see the supplementary material).

3.3. Independent predictors of in-hospital mortality and comparison of mortality rate, length of stay and total charges between arrhythmia and non-arrhythmia-associated hospitalizations

The crude in-hospital mortality was 4.3% in the entire cohort. In univariate analysis, arrhythmias (all combined) were associated with increased in-hospital mortality; crude mortality was 5.4 versus 3.3% for arrhythmia and non-arrhythmia groups, respectively (p < 0.001). After age adjustment, mortality was 4.17% in the arrhythmia group and 4.06% in the non-arrhythmia group.

In multivariate mixed-effect logistic regression analysis, cardiac arrest was associated with increased in-hospital mortality (Table 2a). Dysrhythmia and conduction disorders were not associated with increased in-hospital mortality. Table 2a shows the full list of all variables included in the logistic model. When individual arrhythmias/conduction disorders

Please cite this article as: S. Sulaiman, N. Yousef, M.M. Mehanni, et al., Burden of arrhythmia and electrophysiologic procedures in alcoholic cardiomyopathy hospitalizations, International Journal of Cardiology, https://doi.org/10.1016/j.ijcard.2020.01.068

2

Table 1

Baseline patient and hospital-level characteristics of primary and secondary alcoholic CMP hospitalizations per arrhythmia status.

	All N = 75,430	No-arrhythmia N = 39,123	Arrhythmia N = 36,307	p value
Age in years mean (95% CI)	54.95 (±0.22)	53.2 (±0.7)	56.9 (±0.3)	< 0.001
Male %	85.4%	81.9%	89.5%	<0.0001
Race %	03.4/0	01,5%	05.5%	< 0.0001
White	55.1	50.6	60.2	<0.001
Black		23.9		
	20.3		16.1 7.2	
Hispanic Others (in the diamonical in the	7.4	7.6		
Others (including missing data)	17.2	17.8	16.4	
Hospital region %				0.0001
Northeast	23.8	23.5	24.3	
Midwest	23.4	23.7	22.9	
South	30.8	32.1	29.3	
West	22	20.7	23.5	
Hospital bed size %				0.277
Small	13.4	12.9	13.8	
Medium	26.3	26.5	26.1	
Large	60.3	60.5	60.1	
Hospital location/teaching status %				0.06
Rural	10.2	10.6	9.6	
Urban non-teaching	39.8	39.1	40.7	
Urban teaching	50	50.2	49.7	
Median household income for patient's zip code %	50	50.2	15.7	<0.001
0–25th percentile	32.6	35.2	29.6	
26–50th percentile (median)	26.2	26.4	25.9	
51–75th percentile	22.4	21.7	23.2	
75–100th percentile Others	18.9	16.8	21.3	
Primary payer % (insurance)				< 0.001
Medicare	33.6	31.6	35.8	
Medicaid	22.7	25.2	19.8	
Private insurance	24.3	23.1	25.7	
Self-pay	13.6	14.1	13	
Others	5.9	6	5.7	
CHF %	29.9	31.6	28.2	< 0.001
Chronic lung disease %	27.2	27.1	27.3	0.69
Coagulopathy %	14.4	14.8	13.9	0.03
CVA	2.5	2.2	2.8	0.01
DM %	2.5 16.2	2.2 16.7	2.8 15.6	0.01
Drug abuse %	10.2	11.6	9	< 0.001
Hypertension %	51.2	51.2	9 51.2	<0.001 0.97
Liver disease %	20	21.4		
			18.5	< 0.001
Obesity %	9.1	7.6	10.8	< 0.001
Renal failure%	11.5	11.6	11.3	0.55
Respiratory failure %	16	14.2	18	< 0.001
Sepsis %	8	8.2	7.8	0.39
Shock %	5.6	4.5	6.7	< 0.001

(SAN, SVT, AFib/AFL, 1st degree AV block/Mobitz I, CHB, VT and VFIB) were used in multivariate regression model, none except VFIB were statistically significant (Table 2b).

The overall median (and IQR) length of hospital stay was 4 (6) days. The median (and IQR) length of stay in the arrhythmia vs nonarrhythmia groups was 5 (5) vs 4 (5), respectively (p < 0.001). The overall median (IQR) hospital charge for hospitalization with ACMP was \$27,114 (42,154). The median (and IQR) total charge in the arrhythmia vs non-arrhythmia groups were \$31,127 (49,944) vs \$24,199 (36,068), respectively (p < 0.001).

3.4. Inpatient utilization of electrophysiological procedures

EP procedures were performed in 5.5% of all hospitalizations overall. This rate was 5.2% in 2007, peaked at 6.5% in 2010, was lowest (4.4%) in 2011 and then increased to 6% in 2014 (p = 0.12) (Fig. 2). The most common procedure was cardioversion (2.7% of total hospitalizations)

followed by ICD placement (2.2%) and PPM placement (1%). Cardioversion increased from 2.3% in 2007 to a peak of 3.6% in 2014 (p = 0.08). An ICD was placed in 2.2% of total hospitalizations; this rate peaked at 3% in 2010 and then decreased to 1.9% in 2014 (p < 0.01). The PPM placement rate was 0.8% in 2007, peaked at 1.5% in 2010 and decreased to 0.6% in 2014 (p < 0.05) (see the supplementary material). Ablation procedures were performed in 0.55% of all hospitalizations; (0.53% were catheter ablations and 0.02% were surgical ablations). AFib/AFL was the most common indication (70.9% of all ablation procedures), see the supplementary material. CIEDs in situ were present in 9.4% of hospitalizations and PPM with AICD (0.3%).

4. Discussion

In this real-world study on a national cohort of 75,430 alcoholic CMP hospitalizations, approximately 48% of these hospitalizations had a codiagnosis of arrhythmias, and atrial fibrillation/flutter was the most common arrhythmia (31.5% of hospitalizations). The presence of arrhythmias was associated with longer hospital stays and higher total charges, but not higher mortality, except for the expected higher mortality in those with cardiac arrest/VF. In addition, an increasing burden of arrhythmia especially atrial fibrillation was observed between 2007 and 2014. Furthermore, a declining rate of ICD and PPM placements was noted over the same period.

Alcohol remains a major public health problem in the US. Approximately 14% of US adults who were surveyed in 2012-2013 had an alcohol use disorder in the preceding year; the prevalence was higher in males, Whites, Native Americans, younger adults and low-income individuals and the condition often went untreated [7]. Approximately one third of asymptomatic alcoholic men or women have evidence of cardiomyopathy [8]. Chronic excessive alcohol consumption causes cardiac toxicity with subsequent cardiomyopathy through different mechanisms, such as mitochondrial dysfunction, increased oxidative stress, decreased protein synthesis, and derangement of fatty acid metabolism in cardiomyocytes, and increased apoptosis by activation of the local RAS system [9]. In addition to these mechanisms, a genetic etiology has been described in a proportion of ACMP patients [10]. ACMP is characterized by LV or biventricular dilatation and impaired contraction along with thin or normal thickness ventricular walls. Although the symptoms and signs are not specific, a long history of alcohol abuse and an absence of other causes of heart failure are key clues to diagnosis. Recovery of the left ventricular function after abstinence of alcohol may support the diagnosis, however, it only occurs in approximately onethird of ACMP patients [11]. Alcohol induces cardiac arrhythmias by causing electrolyte disorders, QT prolongation, adrenergic hyperactivity, decreased heart rate variability and baroreceptor sensitivity [12]. Atrial and ventricular arrhythmias have been reported in patients with ACMP; however, all previous studies have involved small cohorts, and none have been on a national level. Using this large NIS database, we report the largest study to date investigating the frequency of different arrhythmia and electrophysiological procedures in this population.

Arrhythmias were the cause of admission in about 10% of hospitalizations in this cohort in contrast to only 2.6% in the general population. About two thirds of the admissions were caused by non-cardiac diseases highlighting the high degree of comorbidity in this population.

Atrial fibrillation/flutter was the most common arrhythmia (31.5%) in our cohort; its prevalence increased between 2007 and 2014. The high prevalence of AFib/AFL has a significant clinical implication as it indicates that about a third of ACMP patients might need anticoagulation which is challenging in this population that have excessive alcohol intake. In a study that followed 94 patients with ACMP, atrial fibrillation was present in 34% of cases [13]. Alcohol intake is associated with an increased risk of atrial fibrillation through progressive atrial remodeling secondary to direct alcohol toxicity and other contributions of alcohol to LV remodeling/cardiomyopathy, hypertension, obesity, and obstructive

S. Sulaiman et al. / International Journal of Cardiology xxx (xxxx) xxx

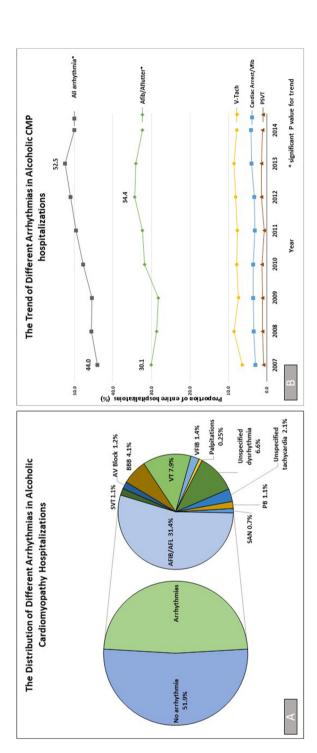




Table 2a

Independent predictors of in-hospital mortality in Alcoholic cardiomyopathy hospitalizations.

	OR	Lower 95% CI	Upper 95% CI	p value
Statistically significant predictors (ordered from the higher to lower OR)				
Cardiac arrest	12.2	8.4	17.8	< 0.001
Respiratory failure*	8.2	6.3	10.6	< 0.001
Shock	3.2	2.3	4.6	< 0.001
Tumors w/wo metastases*	3.1	2	4.9	< 0.001
Renal failure [*]	2.1	1.5	2.9	< 0.001
Sepsis	2.0	1.4	2.8	< 0.001
Liver disease*	1.8	1.4	2.3	< 0.001
Age (every 10 years)*	1.3	1.2	1.5	< 0.001
Hypertension	0.5	0.4	0.6	< 0.001
Hosp location/teaching				
Rural (reference)				
vs urban nonteaching	0.6	0.4	0.8	0.002
vs urban teaching*	0.5	0.3	0.7	< 0.001

Statistically insignificant predictors that were adjusted for in this model included: sex, race, dysrhythmia, conduction disorders, ICD in situ, PPM in situ, CHF, primary cardiac diagnosis, PVD, CVA, pulmonary circulation disorders, chronic lung disease, DM, hypothyroidism, weight loss, obesity, electrolytes disorders, AIDS, coagulopathy, anemia, drug abuse, depression, psychosis, hospital characteristics, median household income, primary payer and weekend vs weekday admission.

Significant p value.

sleep apnea [14]. Independent predictors of atrial fibrillation in our cohort were: age, male sex, Caucasian race, hypothyroidism, sleep apnea and obesity. In our cohort, sleep apnea increased from 2.9% to 7.3% (between 2007 and 2014, p < 0.001), and a similar trend in obesity was observed (5.9% in 2007 and 12.7% in 2014, p < 0.001). These trends may explain the increase in atrial fibrillation in our cohort (see the supplementary material).

The cardiac arrest/ventricular fibrillation prevalence was 3.5% in our study. In the above-mentioned study of 94 patients with ACMP, during a median follow up of 59 months, 9% had sudden cardiac death, and 4.2% were resuscitated from ventricular fibrillation [13]. The difference in the prevalence between both studies is likely explained by the fact that our study is only observing in-hospital cardiac arrest whereas the previous study has likely reported both in-hospital and out-of-hospital cardiac arrests.

In our study, electrolyte disorders, LBBB and the Southern/Western US regions were independently associated with an increased risk of cardiac arrest. In a study by Guzzo-Merello et al., LBBB was found to be an independent predictor of malignant ventricular arrhythmia in patients with ACMP [15]. The western US has the highest per capita ethanol consumption [16]. The largest gap in the treatment of substance abuse in the US exists in the southern and southwestern states [17]. In our study, smoking and depression were associated with a lower risk of

Table 2b

Individual arrhythmias/conduction disorders as predictors of in-hospital mortality in a multivariate logistic model. The same confounders in Table 2a were included except for cardiac arrest, dysrhythmia and conduction disorders which were replaced by individual disorders.

Predictors (individual	OR	Lower	Upper	р
arrhythmias/conduction		95% CI	95% CI	value
disorders)				
VFIB*	3.8	2.2	6.5	< 0.001
VT	0.9	0.6	1.4	0.766
SVT	1.6	0.8	3.3	0.207
AFIB/AFL	0.7	0.6	1.0	0.019
SA node dysfunction	0.5	0.1	2.6	0.447
1st degree AV block/MOBITZ1	1.0	0.3	3.1	0.983
Complete heart block	0.8	0.2	3.7	0.816
LBBB	0.5	0.2	1.1	0.088
ICD in situ	1.2	0.8	1.8	0.414
PPM in situ	0.8	0.3	2.1	0.66

Significant *p* value.

cardiac arrest. Previous studies have shown that patients with substance use disorder and associated mental distress are more likely to seek medical care than those who do not have mental symptoms [18], thus potentially explaining the lower risk of cardiac arrest among patients with comorbid depression in our cohort. A smoking paradox defined as lower mortality after myocardial infarction in smokers has been described in previous studies and has been attributed to the association of smoking with younger age and lower prevalence of other risk factors [19]. The persistent association of smoking with lower in-hospital cardiac arrest in our study despite adjustment for age and other comorbidities probably represents residual unmeasured confounding.

Other traditional risk factors for cardiac arrest in the general population were not associated with an increased risk of cardiac arrest in our alcoholic CMP subjects (hypertension, dyslipidemia, DM, male sex and obesity). These risk factors are likely to increase the risk of cardiac arrest in the general population by increasing the risk of CAD. However, patients with a history of CAD were excluded from our cohort (by definition).

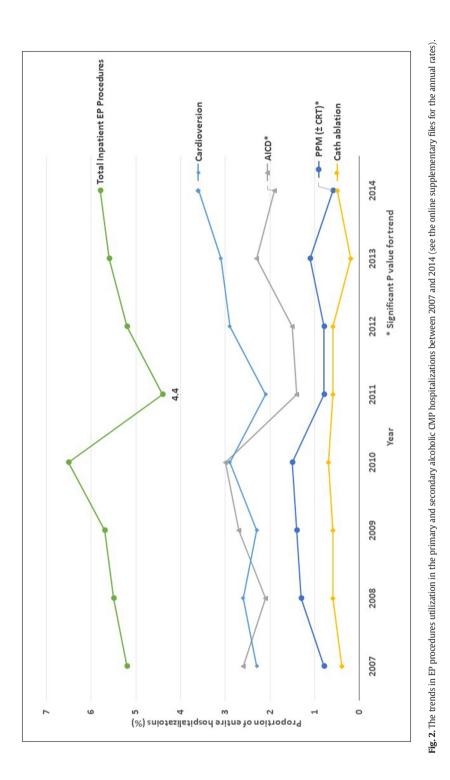
Cardiac arrest (including VFIB) was associated with higher inhospital mortality. Conduction disorders or dysrhythmia (combined or as individual disorders) were not associated with increased mortality. Notably, our study investigated in-hospital mortality and not intermediate or long-term mortality, as previous studies have investigated. Studies regarding the long-term prognosis of ACMP have been conflicting; the survival rate has been reported to be 50% in abstainers and 30% in persistent drinkers over a median follow up of 4 to 5 years [1,20,21]. In one study, atrial fibrillation, QRS width > 120 ms, and an absence of beta-blocker therapy were found to be independent predictors of death or heart transplantation [13].

To our knowledge, this is the first study examining the use of different EP procedures in patients with alcoholic cardiomyopathy on a national level. New ICD placement occurred in 2.2% of hospitalizations. In the study by Guzzo-Merello et al., during a median follow up of 59 months of 94 patients with ACMP, with an average LV ejection fraction (26 \pm 9), most of whom had NYHA functional status II–IV, 33% of patients received an ICD and 19.1% received cardiac resynchronization therapy [13]. In our population, the ICD placement rate decreased from 2007 to 2014 and was lowest in 2011-2012 mirroring the national trend of ICD utilization in general population. ICD implantation in the US decreased between 2006 and 2011 because of increasing concern about the safety of some ICD devices that had been recalled and the inappropriate use of ICDs that led to investigations by the Department of Justice in 2012 [22-24]. Another factor that is likely to affect the placement of ICD is insurance status. An increasing share of Medicaid insurance was observed in our population (19.9% in 2010 and 29.4% in 2014), which was probably secondary to the advent of the Affordable Care Act in 2010. Previous studies have shown that a lack of insurance is associated with underutilization of ICD in eligible candidates [22,25]. The change in insurance composition in our population may partially explain the recovering increasing rate of ICD placement in 2013 and 2014, owing to the decreasing proportion of uninsured patients.

In our cohort, PPM implantation varied over the years, peaked in 2010 and significantly decreased in 2011–2012. The annual pacemaker implantation rate in United States plateaued between 2001 and 2009 [26] and subsequently showed a precipitous decrease in in-hospital PPM placement between 2009 and 2013 [27], which was probably secondary to the above mentioned federal inquiries that scrutinized dual-chamber pacemakers in addition to the ICDs, and to the possibility that more pacemakers may be implanted in outpatient settings.

Our study did not include data on the amount of alcohol consumed by these patients. The NIS is based on administrative data and is predisposed to coding inaccuracy. The NIS captures hospitalizations and not patients themselves; as such, we cannot rule out the possibility that the same patient might be admitted multiple times. A considerable portion of arrhythmias is reported as unspecified. Information about race was missing in approximately 15% of observations; however,

S. Sulaiman et al. / International Journal of Cardiology xxx (xxxx) xxx



S. Sulaiman et al. / International Journal of Cardiology xxx (xxxx) xxx

because race was one of multiple predictors herein and not the focus of study, it was not imputed with complex statistical methods. The NIS does not include information on patient medications. Despite these limitations, the large study population and national representativeness make this study one of the largest of real-world sample studies of ACMP to date. Notably, our study was not equipped to identify the pathophysiology underlying different findings and therefore future studies are needed to elucidate these mechanisms.

5. Conclusion

Arrhythmias were reported as a primary or secondary diagnosis in approximately 48% of hospitalizations. Between 2007 and 2014, there was an increasing burden of cardiac arrhythmias secondary to increasing atrial fibrillation. Over the same period, there was a decreasing rate of PPM or ICD placement. Except for cardiac arrest, presence of arrhythmias was not associated with increased in-hospital mortality, but it was associated with longer hospital stay and higher total charges. There is a need to explore preventive and therapeutic strategies to alleviate this health care burden.

Abbreviations

ACMP	alcoholic cardiomyopathy
AFib	atrial fibrillation
AFL	atrial flutter
AICD	automatic implantable cardioverter defibrillator
AV	atrioventricular
AV_BBB	
BBB	bundle branch block
CAD	coronary artery disease
CCS	Clinical Classifications Software
CDC	Centers for Disease Control and Prevention
CHB	complete heart block
CIED	cardiac implanted electronic devices
CMP	cardiomyopathy
COPD	chronic obstructive pulmonary disease
CRT	cardiac resynchronization therapy
EP	electrophysiology
HCUP	HealthCare Utilization Project
ICD	implantable cardiac defibrillator
ICD-9	The International Classification of Diseases, Ninth Revision
IQR	interquartile range
LBBB	left bundle branch block
LOS	length of stay
LV	left ventricle
MI	myocardial infarction
NIS	National Inpatient Sample
OSA	obstructive sleep apnea
PB	premature beats
PPM	permanent pacemaker placement
PSVT	paroxysmal supraventricular tachycardia
SAN	sino-atrial node dysfunction
SVT	supra-ventricular tachycardia
VFIB	ventricular fibrillation
VT	ventricular tachycardia

Disclaimer

The scientific content and discussion of this article reflects the authors' own views and is not an official statement of their respective institutions.

Source of support

No disclosures.

CRediT authorship contribution statement

Samian Sulaiman: Conceptualization, Methodology, Formal analysis, Writing - original draft. Nazdar Yousef: Writing - review & editing. Mina M. Mehanni: Writing - review & editing. Sakthi Sundararajan: Writing - review & editing. Romina Wingert: Writing - review & editing. Michael Wingert: Writing - review & editing. Asim Mohammed: Supervision, Writing - review & editing. Arshad Jahangir: Supervision, Writing - review & editing.

Declaration of competing interest

The authors report no financial relationships or conflicts of interest regarding the content herein.

Acknowledgments

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi. org/10.1016/j.ijcard.2020.01.068.

References

- G. Guzzo-Merello, M. Cobo-Marcos, M. Gallego-Delgado, P. Garcia-Pavia, Alcoholic cardiomyopathy, World J. Cardiol. 6 (8) (2014) 771–781.
- [2] C.W. Yancy, M. Jessup, B. Bozkurt, J. Butler, D.E. Casey Jr., M.H. Drazner, et al., 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, Journal of the American College of Cardiology 62 (16) (2013) e147–e239.
- [3] Project HCaU, HCUP NIS Database Documentation, Available from: www.hcup-us. ahrq.gov/db/nation/nis/nisdbdocumentation.jsp 2018.
- [4] StataCorp, Stata Statistical Software: Release 15, 2017.
- [5] Team RC, R: A Language and Environment for Statistical Computing, 2018.
- [6] United States Department of Health and Human Services (US DHHS) CfDCaP, (CDC) NCfHSN, Bridged-Race Population Estimates, United States July 1st Resident Population by State, County, Age, Sex, Bridged-race, and Hispanic Origin [Compiled from 1990–9 bridged-race Intercensal Population Estimates (Released by NCHS on 7/26/2004); Revised Bridged-race 0–9 Intercensal Population Estimates (Released by NCHS on 10/26/12); and Bridged-race Vintage 17 (10–17) Postcensal Population Estimates (Released by NCHS on 6/27/18). Available on CDC WONDER Online Database.], Available from: http://wonder.cdc.gov/bridged-race-v2017.html.
- [7] B.F. Grant, R.B. Goldstein, T.D. Saha, S.P. Chou, J. Jung, H. Zhang, et al., Epidemiology of DSM-5 alcohol use disorder: results from the National Epidemiologic Survey on Alcohol and Related Conditions III, JAMA Psychiatry. 72 (8) (2015) 757–766.
- [8] A. Urbanon-Marquez, R. Estruch, J. Fernandez-Sola, J.M. Nicolas, J.C. Pare, E. Rubin, The greater risk of alcoholic cardiomyopathy and myopathy in women compared with men, Jama. 274 (2) (1995) 149–154.
- [9] M.R. Piano, S.A. Phillips, Alcoholic cardiomyopathy: pathophysiologic insights, Cardiovasc. Toxicol. 14 (4) (2014) 291–308.
- [10] J.S. Ware, A. Amor-Salamanca, U. Tayal, R. Govind, I. Serrano, J. Salazar-Mendiguchia, et al., Genetic etiology for alcohol-induced cardiac toxicity, J. Am. Coll. Cardiol. 71 (20) (2018) 2293–2302.
- [11] A. Mirijello, C. Tarli, G.A. Vassallo, L. Sestito, M. Antonelli, C. d'Angelo, et al., Alcoholic cardiomyopathy: what is known and what is not known, European Journal of Internal Medicine. 43 (2017) 1–5.
- [12] A. George, V.M. Figueredo, Alcohol and arrhythmias: a comprehensive review, Journal of Cardiovascular Medicine (Hagerstown, Md) 11 (4) (2010) 221–228.
- [13] G. Guzzo-Merello, J. Segovia, F. Dominguez, M. Cobo-Marcos, M. Gomez-Bueno, P. Avellana, et al., Natural history and prognostic factors in alcoholic cardiomyopathy, JACC Heart Failure 3 (1) (2015) 78–86.
- [14] A. Voskoboinik, S. Prabhu, L.H. Ling, J.M. Kalman, P.M. Kistler, Alcohol and atrial fibrillation: a sobering review, J. Am. Coll. Cardiol. 68 (23) (2016) 2567–2576.
- [15] G. Guzzo-Merello, F. Dominguez, E. Gonzalez-Lopez, M. Cobo-Marcos, M. Gomez-Bueno, I. Fernandez-Lozano, et al., Malignant ventricular arrhythmias in alcoholic cardiomyopathy, Int. J. Cardiol. 199 (2015) 99–105.
- [16] S.P.S. Haughwout, E. Megan, Apparent Per Capita Alcohol Consumption: National, State, and Regional Trends, 1977–2016, National Institute on Alcohol Abuse and Alcoholism. Division of Epidemiology and Prevention Research. Alcohol Epidemiologic Data System, April 2018 Report No.: Surveillance report #110.
- [17] W.E. McAuliffe, R. Dunn, Substance abuse treatment needs and access in the USA: Interstate variations, Addiction 99 (2004) 999–1014PMID: 15265097.
- [18] L.A. Schmidt, Recent developments in alcohol services research on access to care, Alcohol Research: Current Reviews 38 (1) (2016) 27–33.

8

ARTICLE IN PRESS

S. Sulaiman et al. / International Journal of Cardiology xxx (xxxx) xxx

- [19] S.F. Ali, E.E. Smith, M.J. Reeves, X. Zhao, Y. Xian, A.F. Hernandez, et al., Smoking paradox in patients hospitalized with coronary artery disease or acute ischemic stroke: findings from get with the guidelines, Circulation Cardiovascular Quality and Outcomes. 8 (6 Suppl 3) (2015) S73–S80.
- [20] L. Fauchier, D. Babuty, P. Poret, D. Casset-Senon, M.L. Autret, P. Cosnay, et al., Comparison of long-term outcome of alcoholic and idiopathic dilated cardiomyopathy, Eur. Heart J. 21 (4) (2000) 306–314.
- [21] A. Gavazzi, R. De Maria, M. Parolini, M. Porcu, Alcohol abuse and dilated cardiomy-opathy in men, Am. J. Cardiol. 85 (9) (2000) 1114–1118.
 [22] N.J. Patel, S. Edla, A. Deshmukh, N. Nalluri, N. Patel, K. Agnihotri, et al., Gender, racial,
- [22] N.J. Patel, S. Edla, A. Deshmukh, N. Nalluri, N. Patel, K. Agnihotri, et al., Gender, racial, and health insurance differences in the trend of implantable cardioverterdefibrillator (ICD) utilization: a United States experience over the last decade, Clin. Cardiol. 39 (2) (2016) 63–71.
- [23] S.M. Al-Khatib, A. Hellkamp, J. Curtis, D. Mark, E. Peterson, G.D. Sanders, et al., Non-evidence-based ICD implantations in the United States, Jama. 305 (1) (2011) 43–49.

- [24] J.S. Steinberg, S. Mittal, The federal audit of implantable cardioverterdefibrillator implants: lessons learned, J. Am. Coll. Cardiol. 59 (14) (2012) 1270-1274.
- [25] N.M. LaPointe, S.M. Al-Khatib, J.P. Piccini, B.D. Atwater, E. Honeycutt, K. Thomas, et al., Extent of and reasons for nonuse of implantable cardioverter defibrillator devices in clinical practice among eligible patients with left ventricular systolic dysfunction, Circulation Cardiovascular Quality and Outcomes. 4 (2) (2011) 146–151.
- [26] A.J. Greenspon, J.D. Patel, E. Lau, J.A. Ochoa, D.R. Frisch, R.T. Ho, et al., Trends in permanent pacemaker implantation in the United States from 1993 to 2009: increasing complexity of patients and procedures, J. Am. Coll. Cardiol. 60 (16) (2012) 1540–1545.
- [27] A. Guha, X. Xiang, D. Haddad, B. Buck, X. Gao, M. Dunleavy, et al., Elevenyear trends of inpatient pacemaker implantation in patients diagnosed with sick sinus syndrome, J. Cardiovasc. Electrophysiol. 28 (8) (2017) 933–943.