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Journal of Cardiology & Current Research

Research Article

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Characteristics and outcomes of Marijuana users admitted with sudden cardiac arrest

Abstract

Background: Marijuana or Cannabis is the most commonly used illicit drug in the United States. An estimated 2 million adults who reported marijuana use also have cardiovascular disease. Marijuana use has been associated with acute myocardial infarction, heart failure and arrhythmias. However, the implications of marijuana use on sudden cardiac arrest outcomes is unknown.

Methods: Using the National Inpatient Sample of the years 2018 & 2019, patient characteristics and in-hospital outcomes were compared between marijuana users and non-marijuana users admitted with sudden cardiac arrest.

Results: The median age of marijuana users was lower at 46.8years. They had significantly lower prevalence of congestive heart failure, coronary artery disease, valvular heart disease, pulmonary circulation disorders, atrial fibrillation, hypertension, and diabetes and a significantly higher prevalence of chronic liver disease, depression, alcohol use, tobacco use, amphetamine/psychostimulant use, opioid use, cocaine use, and sedative use. Multivariable logistic regression analysis showed significantly higher odds for ventricular fibrillation (OR: 1.24; 95% CI: 1.09- 1.41; p- 0.001) but lower odds for mortality (OR: 0.86; 95% CI: 0.78- 0.96; p-0.011), need for mechanical ventilation (OR: 0.76; 95% CI: 0.67-0.86; p- 0.000), and tracheostomy (OR: 0.46; 95% CI: 0.34- 0.62; p- 0.000). Marijuana users were also more likely to be discharged home with self-care (25.25% vs 11.53%).

Conclusion: Among patients admitted with sudden cardiac arrest, marijuana users were found to have significantly higher odds for ventricular fibrillation. They were found to have lower odds for in-hospital mortality, mechanical ventilation, and tracheostomy and were more likely to be discharged home with selfcare, but this is mostly because marijuana users who are admitted with sudden cardiac arrest were younger and had considerably fewer chronic medical conditions. Large prospective cohort studies are needed to ascertain the health risks associated with marijuana use.

Keywords: marijuana use, sudden cardiac arrest, food and drug administration

Volume 16 Issue 1 - 2023

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Received: January 17, 2022 | **Published:** February 10, 2023

Abbreviations: FDA, food and drug administration; THC, tetrahydrocannabinol; CBD, cannabidiol; SCA, sudden cardiac arrest; NIS, national inpatient sample; AHA, American heart association

Introduction

Marijuana or Cannabis is the most commonly used illicit drug in the United States and about 48.2million people or 18% of Americans used it at least once in 2019.[1] Marijuana remains a Schedule 1 controlled substance by Federal law, but currently 19 states, two territories and the District of Columbia allow recreational use.[2] This change has resulted in increased use of marijuana with its greatest use seen in young adults.[3] While marijuana is mostly used recreationally, medical use of marijuana is approved by the U.S Food and Drug Administration (FDA) for rare forms of epilepsy (cannabidiol), refractory chemotherapy- associated nausea and vomiting (dronabinol and nabilone) and human immunodeficiency induced weight loss (dronabinol).[4] A total of 37 states, three territories and the District of Columbia regulate marijuana for medical use by qualified individuals[1]. But despite the widespread use of marijuana, our knowledge of its health implications is limited.

The physiological effects of marijuana are derived from its active compounds called cannabinoids, of which the most common are the delta-9-tetrahydrocannabinoid (THC) and the cannabidiol (CBD).[5] They act on the endocannabinoid system that has two CBD receptors-CB1 and CB2. CB1 receptors are present in high concentrations in the central and peripheral nervous system but is also seen in platelets, myocytes, adipose tissue, liver, pancreas, and skeletal muscle. CB2 receptors are present on immune cells, osteoclasts and osteoblasts[6]. Through these receptors, the endocannabinoid system can impact multiple organ systems.

An estimated 2million adults who reported marijuana use also have cardiovascular disease.[7] Marijuana use has been associated with acute myocardial infarction, heart failure and arrhythmias.[8–11] However, the implications of marijuana use on sudden cardiac arrest outcomes is unknown. Sudden Cardiac Arrest (SCA) is a public health concern that accounts for 15-20 % of all deaths and ~50% of all cardiovascular deaths.[12] It is also estimated that 50% of SCA's occur in individuals without a previously diagnosed heart disease.[12,13] With reports of association of marijuana use and acute myocardial infarction and arrhythmias, it is imperative that we explore the role of marijuana use in sudden cardiac arrest. In this study, we seek to identify characteristics of patients with marijuana use admitted with sudden cardiac arrest and assess in-hospital outcomes.

Methods

Data for this study was obtained from the National Inpatient Sample (NIS) of the years 2018 & 2019. NIS was made possible by a Federal-State-Industry partnership sponsored by the Agency

for Healthcare Research and Quality (AHRQ). The database was designed to approximate a 20% stratified sample of U.S hospitals representing more than 95% of the U.S population (including urban and rural hospitals across all geographic locations). Statistical sampling weights provided by the NIS allow extrapolation to c. Owing to the de-identified nature of the dataset, informed patient consent or institutional review board approval was not required for this study.

The study population included patients with documented history of marijuana use admitted with sudden cardiac arrest. They were identified using the International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10 CM) codes. ICD-10 code F12 was used for marijuana use and I46 used to ascertain cardiac arrest patients. Only patients 18years and older were included in the study population. The full list of ICD-10 codes used in the study is given in the supplement. The following baseline characteristics were obtained: age, sex, median household income percentile, history of congestive heart failure, coronary artery disease, valvular heart disease, pulmonary circulation disorders, chronic pulmonary disease, atrial fibrillation, hypothyroidism, chronic kidney disease, chronic liver disease, metastatic cancer, coagulopathy, obesity, hypertension, diabetes, depression, amphetamine/psychostimulant use, hallucinogen use, opioid use, cocaine use, sedative use, tobacco use, and alcohol use. The following in-hospital outcomes were compared between the marijuana users and non-marijuana users: mortality, length of stay, ventricular fibrillation, ventricular tachycardia, mechanical ventilation, PEG placement, tracheostomy, vasopressor use, stroke, pneumonia, pulmonary embolism, and discharge disposition.

Descriptive statistics were presented as frequencies with percentages for categorical variables and as median for continuous variables. Baseline characteristics were compared using a Pearson chi-squared test and Fisher's exact test for categorical variables and independent samples t-test for continuous variables. Outcomes were compared using linear and logistic regression analyses for continuous and binary variables respectively. Univariate regression was carried out first and multivariate regression (adjusted for age, race, sex, Elixhauser co-morbidity index, hospital size, hospital location, amphetamine/psychostimulant use, hallucinogen use, opioid use, cocaine use, sedative use, tobacco use, and alcohol use) conducted when p-value was <0.2 after univariate analysis. A p value of < 0.05 was considered statistically significant. Discharge disposition being a categorical variable was compared using Chi-squared test. Because of the complex survey design of the NIS data, sample weights, strata and clusters were applied to raw data to generate national estimates. Statistical analysis was conducted using Stata (College Station, Texas, USA) version 17.0. The Stata survey data command "svy" was used for analysis.

Results

A total of 426,080 hospitalizations for cardiac arrest were identified, of which 7575 had history of marijuana use. Baseline characteristics of the marijuana users and non-marijuana users admitted with cardiac arrest is given in Table 1. Patients in the marijuana user group were younger with a median age of 46.8 years (46.09- 47.5) vs 66.1 years (65.9-66.24) in the non- marijuana user group. The percentage of females was lower in the marijuana user group (30.6% vs 42.7%), and they also had a lower median household income (37.7% vs 33.7% in the < 25th percentile of median household income). Marijuana users had significantly lower prevalence of congestive heart failure (33.8% vs 44.2%), coronary artery disease (22.24% vs 34.2%), valvular heart disease (8.58% vs 12.17%), pulmonary circulation disorders (8.98% vs 12.49%), atrial fibrillation (15.58% vs 28.67%), hypothyroidism (5.28% vs 12.22%), chronic kidney disease (15.64% vs 32.25%), metastatic cancer (2.44% vs 4.92%), obesity (12.81% vs 15.88%), hypertension (51.62% vs 69.59%), and diabetes (19.08% vs 37.41%). They had a significantly higher prevalence of chronic liver disease (24.49% vs 17.45%), depression (16.3 % vs 9.81%), alcohol use (22.11% vs 6.21%), tobacco use (3.76% vs 1.59%), amphetamine/psychostimulant use (3.04% vs 0.34%), hallucinogen use (0.66% vs 0.0043%), opioid use (11.35% vs 1.34%), cocaine use (20.07% vs 1.38%), and sedative use (5.35% vs 0.29%). The prevalence rates of chronic pulmonary disease (28.45% vs 28.2%) and coagulopathy (18.75% vs 18.68%) were similar in both groups.

Table 1 Baseline Characteristics (in %)

Median Age (in years)	**46.8 (46.09-47.5)**	**66.1 (65.9-66.24)**	**0.000**
18 - < 50years (in %)	53.79	14.38	
50 - < 65years	34.9	27.45	
65 - < 75years	9.5	25.13	
> 75years	1.7	33.02	
Female	30.63	42.7	0.000
Median household Income Percentile			
0- 25th	37.7	33.7	0.000
26- 50th	27.95	26.18	
51- 75th	20.04	22.62	
76- 100th	14.31	17.5	
Congestive Heart Failure	33.8	44.21	0.000
Coronary Artery Disease	22.24	34.21	0.000
Valvular Disease	8.58	12.17	0.000
Pulmonary Circulation Disorders	8.98	12.49	0.000
Peripheral Vascular Disease	8.05	11.2	0.000
Chronic Pulmonary Disease	28.45	28.2	0.82
Atrial Fibrillation	15.58	28.67	0.000
Hypothyroidism	5.28	12.22	0.000
Chronic Kidney Disease	15.64	32.25	0.000
Chronic Liver Disease	24.49	17.45	0.000
Metastatic Cancer	2.44	4.92	0.000
Coagulopathy	18.75	18.68	0.94
Obesity	12.81	15.88	0.001
Hypertension	51.62	69.59	0.000
Diabetes Mellitus	19.08	37.41	0.000
Anemia	5.41	5.42	0.99
Depression	16.3	9.81	0.000
Amphetamine & Psychostimulant Use	3.04	0.34	0.000
Hallucinogen Use	0.66	0.0043	0.000
Opioid Use	11.35	1.34	0.000
Cocaine Use	20.07	1.38	0.000
Sedative Use	5.35	0.29	0.000
Tobacco Use	3.76	1.59	0.000
Alcohol Use	22.11	6.21	0.000

In-hospital outcomes are given in Tables 2 & 3. On univariate analysis, there was no significant difference in median length of stay (8.1 vs 8.5 days; p-0.3), PEG placement (0.066% vs 0.15%; p-0.38), tracheostomy (3.36% vs 4.37%; p- 0.05), vasopressor use (12.01% vs 12.81%; p- 0.36), pneumonia (71.28% vs 69.85%; p- 0.21) and pulmonary embolism (3.69% vs 4.27%; p- 0.26). It was significant for mortality (48.77% vs 60.68%; p- 0.000), ventricular fibrillation (22.31% vs 15.78%; p- 0.000), ventricular tachycardia (17.68% vs 14.91%; p- 0.004), mechanical ventilation (75.44% vs 67.92%; p- 0.000) and stroke (97.95% vs 98.76%; p- 0.005). On multivariable analysis, there was no significant differences in stroke (OR: 0.86; 95% CI: 0.57-1.28; p-0.46) and in ventricular tachycardia (OR: 1.11; 95% CI: 0.96-1.29; p- 0.133). It showed significantly higher odds for

ventricular fibrillation (OR: 1.24; 95% CI: 1.09- 1.41; p- 0.001) but lower odds for mortality (OR: 0.86; 95% CI: 0.78- 0.96; p- 0.011), need for mechanical ventilation (OR: 0.76; 95% CI: 0.67- 0.86; p- 0.000), and tracheostomy (OR: 0.46; 95% CI: 0.34- 0.62; p- 0.000). Marijuana users were more likely to be discharged home with self-care (25.25% vs 11.53%), less likely to be discharged to a skilled nursing facility or other similar facility (13.75% vs 17.42%) and more likely to sign out against medical advice (2.38% vs 0.45%) (Supplementary Table).

Table 2 In-hospital Outcomes (in %)

	Marijuana Users	Non-Marijuana Users	p-value (unadjusted)
Mortality	48.77	60.68	0.000
Median Length of Stay	8.1days	8.5days	0.318
Ventricular Fibrillation	22.31	15.78	0
Ventricular Tachycardia	17.68	14.91	0.004
Mechanical Ventilation	75.44	67.92	0.000
PEG	0.066	0.15	0.38
Tracheostomy	3.36	4.37	0.05
Vasopressor Use	12.01	12.81	0.36
Stroke	97.95	98.76	0.005
Pneumonia	71.28	69.86	0.21
Pulmonary Embolism	3.69	4.27	0.26
Discharge Disposition			
Home/ Self Care	25.25	11.53	0.000
Short Term Hospital	4.56	4.38	
SNF, Another Type of Facility	13.75	17.42	
Home Health Care	5.29	5.41	
Against Medical Advice	2.38	0.45	

Table 3 Adjusted In-hospital Outcomes

	Odd's Ratio	p-value
Mortality	0.86 (0.78- 0.96)	0.011
Ventricular Fibrillation	1.24 (1.09- 1.41)	0.001
Ventricular Tachycardia	1.11 (0.96-1.29)	0.133
Mechanical Ventilator	0.76 (0.67-0.86)	0.000
Tracheostomy	0.46 (0.34-0.62)	0.000
Stroke	0.86 (0.57-1.28)	0.46

Supplementary Table

ICD-10 Codes
Marijuana use: F12
Cardiac Arrest: I46
Ventricular Fibrillation: I49
Ventricular Tachycardia: I472
Amphetamine/psychostimulant use: T4362, T4369
Hallucinogen use: F16
Opioid use: F11
Cocaine use: F14
Sedative use: F13
Tobacco use: F17, Z720, Z7722
Alcohol use: F10
Coronary Artery Disease: I25
Atrial Fibrillation: I48
Stroke: I60, I61, I62, I63
Mechanical Ventilator: 5A1935Z, 5A1945Z, 5A1955Z
PEG: 0DH60UZ, 0DH63UZ
Tracheostomy: 0B110F4, 0B110Z4, 0B113F4, 0B113Z4
Vasopressor: 3E033XZ, 3E043XZ
Pneumonia: I26

Discussion

In this study, we found that Marijuana users who were admitted with sudden cardiac arrest were younger, mostly male and had lower median household income. They had significantly fewer chronic medical conditions including hypertension, diabetes, coronary artery disease, atrial fibrillation, and congestive heart failure. They had significantly higher risk of chronic liver disease, depression, and substance abuse such as tobacco use, alcohol use, and illicit drug use such as cocaine, amphetamines, sedatives, and opioids. They had higher odds for ventricular fibrillation but lower odds for in-hospital mortality, mechanical ventilation, and tracheostomy. They were more likely to be discharged home with self-care and more likely to leave against medical advice.

There are several mechanisms by which marijuana can cause adverse cardiovascular effects. Tetrahydrocannabinol (THC) stimulates the sympathetic nervous system, increasing heart rate, myocardial oxygen demand, supine blood pressure and platelet activation. It is also associated with endothelial dysfunction and oxidative stress.[14] Marijuana use has also been associated with myocardial dysfunction, independent of coronary artery disease. Rabbits who received a selective CB2 agonist demonstrated concentration dependent decrease in cardiac contractility.[7,15] The mode of use of marijuana also has an effect on the adverse effects. If marijuana is smoked, it produces a similar array of cardiotoxic chemicals to smoking tobacco[16]. It can also lead to an increase in carbon monoxide in the blood, which is associated with endothelial dysfunction, increased oxidation of lipoproteins, and impaired oxygen binding.[17] But consumption of edibles are associated with increased systemic absorption, slower time to onset and peak effect making it more likely to cause acute adverse effects.[5]

There is observational data that links marijuana use with adverse cardiovascular effects. An increase in cardiac related deaths has been observed in states where marijuana has been legalized.[18] A temporal link between marijuana use and acute coronary syndrome has been observed in a meta-analysis of 36 studies and in the Determinants of Myocardial Infarction Onset Study.[9,19] Marijuana use was associated with twice the hazard of death among patients with first myocardial infarction in patients under 50 years of age in the YOUNG-MI registry.[20] It has also been found to be associated with arrhythmia, mostly atrial fibrillation in 3% of reported cases of marijuana use in a NIS study.[10] Due to the growing evidence of adverse cardiovascular effects from marijuana use, the American Heart Association (AHA) issued a statement in September, 2020 emphasizing the negative health implications of marijuana and has recommended policy makers to limit smoking of any products and to ban marijuana use for the youth.[5]

Our study is the first of its kind to characterize demographics of patients with admitted with sudden cardiac arrest with marijuana use. But our study does suffer from certain limitations. As our study data utilized the national inpatient sample, we were only able to study hospitalized patients. Hence it suffers from selection bias. The marijuana user cohort also had a higher use of tobacco and other substance use. We adjusted for these in the analysis but there could be unidentified confounders that were missed. Our two study cohorts had considerable baseline differences; hence our findings should be interpreted in context. The increased mortality, mechanical ventilation, tracheostomy and need for discharge to skilled nursing in the non-marijuana user group is due to increased baseline age and overall increased chronic medical conditions. Our study does highlight important findings. We noted increased likelihood for ventricular

arrhythmias in the marijuana user group. This finding and that younger people with marijuana use are admitted with cardiac arrest should be considered by health policy makers when legislating marijuana laws. Large scale prospective studies in the general population should be conducted to understand long term effects with marijuana use.

Conclusion

Among patients admitted with sudden cardiac arrest, marijuana users were found to have significantly higher odds for ventricular fibrillation. They were found to have lower odds for in-hospital mortality, mechanical ventilation, and tracheostomy and were more likely to be discharged home with selfcare, but this is mostly because marijuana users who are admitted with sudden cardiac arrest were younger and had considerably fewer chronic medical conditions including hypertension, diabetes, coronary artery disease and congestive heart failure. Marijuana users had a significantly higher prevalence rate of depression and substance abuse including tobacco, alcohol, cocaine, opioid, amphetamine/psychostimulant, and hallucinogen use. Large prospective cohort studies are needed to ascertain the health risks associated with marijuana use.

Acknowledgments

None.

Funding

None.

Conflicts of interest

No conflicts to report.

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