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Adverse Cardiovascular Outcomes in Young Cannabis Users: A Nationwide Analysis

Retrospective Analysis Using the National In-Patient Sample

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Abstract: Background: With the growing trends in recreational marijuana use, our study aims at analyzing the association between Acute coronary syndromes (ACS) and Ventricular Fibrillation (Vfib) and cannabis use disorder in young adults (18 – 45). **Methods**: National In-patient Sample was used for population analysis. Probit logistic regression was used for analyzing the associations between diagnosis of ACS/ Vfib and documented cannabis use disorder. Propensity Score matched samples were made from the ACS/Vfib admissions with Cannabis use disorder to analyze the in-hospital outcomes. **Results**: Statistically significant association was found between admission diagnosis of ACS/ vfib, and documented cannabis use disorder in the study population. The association remained significant after accounting for potential confounders. Documented race as black, documented diagnosis of uncontrolled hypertension and diabetes were found to have significant association with admissions for ACS among the population with documented Cannabis use disorder. No difference in mortality were found between ACS admissions with and without documented cannabis use disorder in the propensity matched cohorts. **Conclusions**: Documented diagnosis of Cannabis use disorder has statistically significant association with admission diagnosis of ACS/Vfib even after accounting for confounders. Documented race as black, and co existing diagnosis of uncontrolled hypertension and diabetes had significant association with admission diagnosis of ACS in population with documented cannabis use disorder.

Keywords: cannabis use disorder; ACS; ventricular fibrillation

1. Introduction

Cannabis use has become widely prevalent throughout society, especially in younger adults amidst recent decriminalization/legalization. Parekh at al found a higher percentage of cannabis users to be less than <34 years of age [1], and a recent NIH monitor the future survey reported an all-time high of young adult marijuana users (age 18-30) in 2021[2]. This alludes to higher tendencies of recreational marijuana use in the young adult population.

Despite its growing prevalence, the physiological effects of cannabis use have not been well studied. Few preliminary studies have advocated for the therapeutic benefit of cannabis for its analgesic and anti-inflammatory effects, reporting that in some experimental models of heart disease cannabidiol downregulates oxidative stress, inflammatory processes and apoptosis [3]. While this may be reassuring, recent research describes detrimental effects of cannabis use. Two separate studies, one using a national inpatient sample from 2007-2014 and the other from 2015-2017, demonstrated statistically significant trends in hypertensive emergency-related admissions in cannabis use disorder despite adjusting for comorbid conditions [4,5]. Cannabis use has also been associated with smoking, and odds of cannabis users **using cocaine have been significant** [6]. Some studies even suggest possible association between cannabis use diabetes via endocannabinoid system modulation [7], and cannabis use and hyperlipidemia via cannabinoid inhibition of reverse cholesterol transport [8].

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Despite these known trends, the available research has few (cohort) studies that focus on cannabis use and cardiovascular trends specifically in the young adult population. A recent Cross-sectional study showed an association between cannabis use and ACS admissions; however, this study utilized self-reported data looking at adults ages 18-74 [9]. One retrospective study demonstrated cannabis use associated with acute-MI from a national inpatient sample from 2010-2014 looking at ages 11-70 [10].

Even fewer studies have looked at cannabis use and ventricular arrhythmias, with one isolated case study describing a patient who had an episode of ventricular fibrillation after smoking more cannabis than his usual (and may be the first ever reported) [11]. To further evaluate the younger population, we looked at the prevalence of acute coronary syndrome and V.fib admissions among young adults with CUD+ (known cannabis use disorder) and non-cannabis users (CUD-) with retrospective analysis of a nationally representative cohort from the United States.

2. Materials and Methods

National Inpatient Sample (2019-2020) was used to analyze the data. ICD10 code trunk 124 was used to select admissions for the diagnosis of acute coronary syndrome. ICD 10 code 14901 was used to select admissions for Ventricular fibrillation. Code trunks F12 and F14 were used to select a documented diagnosis of cannabis use disorder (codes for cannabis use in remission have been avoided). Baseline characteristics of admissions in young adults (18-45) with documented diagnosis of cannabis use was done.CMR comorbidity software and ICD 10 codes were used to select admissions with associated cocaine use, smoking, diabetes and uncontrolled hypertension. Population analysis of admissions for young adults (AGE 18- 45) with acs or vfib and its association with cannabis use disorder was done. Probit logistic regression was used to analyze the association. Adjusted odds ratio was done using probit logistic regression model after accounting for age, sex, race and quarterly income. The comorbidities used in the logistic regression were smoking and cocaine, as these have independent association with cannabis use disorder and acs/ vfib. Co-existing diagnoses of uncontrolled hypertension, diabetes and hyperlipidemia were also included in the multivariate logistic regression as these factors have association with acs/ vfib and are also likely to be prevalent in cannabis use disorder. To analyze the causative effect of cannabis use on adverse outcomes in acs admissions in young adults, a propensity score and nearest neighbor matching (with caliper width of 0.2) was used, were exact matching was done for age, sex, race, quarterly income, prevalence of smoking and cocaine abuse: in hospital outcomes studied were all cause mortality, requirement of intra-aortic balloon pump during the admission, mean length of hospital stay and total hospital charges. P value < 0.05 was used to assess significance in all calculations. Among the admissions with documented cannabis use in young patients, factors that were associated with the diagnosis of ACS were also analyzed.

3. Results

Using the above-mentioned ICD 10 codes, **32990** admissions under the age of 45 for the diagnosis of acs were identified, of which **2295** admissions had documented cannabis use disorder. **1939** admissions under the age of 45, with a diagnosis of ventricular fibrillation were identified, of which **125** admissions had a coexisting diagnosis of cannabis use disorder.

Table 1. Baseline characteristics of Admissions with documented Cannabis use disorder (Age 18 - 45) .

Total Number of Admissions	**543445**	
Mean Age	36.574 (36.023 - 36.897)	
Sex	**Male**	56.17%

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	Female	43.83%
Race	**Whites**	**52.93%**
	Blacks	**28.77%**
	Hispanics	**12.33%**
Quarterly income (calculated from the zip codes of the household)	**1st quartile**	**40.25%**
	2nd quartile	**25.67%**
	3rd quartile	**21%**
	4th quartile	**13.08%**
Hospital Region	**1.Northeast**	**18.02%**
	2. Midwest	**24.9%**
	3.South	**36.64%**
	4.West	**20.44%**
Prevalence of Hypertension	13.86%	
Prevalence of diabetes	5.4%	
Prevalence of Hyperlipidemia	4.40%	
Prevalence of smoking	32.43%	
Prevalence of other drug abuse	64.46%	
Prevalence of Depression/ Psychosis	15.135%	

543445 admissions were identified with documented cannabis use disorder in the age group of 18-45. The prevalence of hypertension, diabetes, hyperlipidemia, smoking, other substance abuse and mental health issues were calculated among the admissions with documented cannabis use using the CMR comorbidity software. .

Table 2. Analysis of acute coronary syndrome and ventricular fibrillation admissions (age 18 - 45) with documented diagnosis of cannabis use disorder .

Young adults (AGE < 45) admitted for-	**Acute coronary syndrome admissions**	**Acute coronary syndrome admissions with cannabis use disorder**	**Ventricular fibrillation**	**Ventricular fibrillation with cannabis use disorder**
Mean Age	**39.83 (38.92 - 40.1)**	**37.76 (37.12 - 37. 85)**	**35.664 (34.93 - 36.39)**	**35.2 (32.38 - 38.017)**
Sex	**Male** 66.93%	**Male** 73. 64%	**Male** **59.96 %**	**Male 56%**

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	Female	33.07%	Female	26.3 6%	Female	43.04 %	Female	44%
Race	Whites	56. 99%	Whites	41.3 7%	Whites	52.38 %	Whites	56%
	Blacks	22.5 4%	Blacks	40.93 %	Blacks	27.51 %	Blacks	32%
	Hispanics	12.6 2%	Hispanics	14.38 %	Hispanics	11.38%	Hispanics	4%
	Others		Others		Others		Others	
Median Household income	1st quartile	36.6%	1st quartile	45.37%	1st quartile	28.08 %	1st quartile	36 %
	2nd quartile	26.36%	2nd quartile	22.69%	2nd quartile	27.82 %	2nd quartile	20%
	3rd quartile	22.69%	3rd quartile	20.26%	3rd quartile	23.1 %	3rd quartile	20 %
	4th quartile	14.3%	4th quartile	11.6%	4th quartile	21%	4th quartile	24 %
Primary Expected Copayer	1.Medicare	8.3%	1.Medicare	9.61%	1.Medicare	9. 59%	1.Medicare	8%
	2. Medicaid	27.88%	2. Medicaid	39.52%	2. Medicaid	30.83%	2. Medicaid	32%
	3.Private Insurance	43.9 %	3.Private Insurance	22.71%	3.Private Insurance	44.3%	3.Private Insurance	40 %
	4. Self Pay	14.68 %	4. Self Pay	23.48 %	4. Self Pay	9.3%	4. Self Pay	8 %
Charlson Comorbidity index (>=5)	11.2%		17.8%		8%		17%	

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Hospital Region	1.Northeast 14.41% 2. Midwest 22.52% 3.South 46.21% 4.West 16.85%	1.Northeast 12.2% 2.Midwest 21.13% 3.South 49.89% 4.West 16.78%	1.Northeast 11.08% 2. Midwest 23.71% 3.South 41.75% 4.West 23.45%	1.Northeast 8% 2. Midwest 32% 3.South 28% 4.West 32%

Table 3. Association between documented diagnosis of cannabis use disorder and admission diagnosis of ACS. (Age 18-45).

Association between acs admissions and cannabis use disorder diagnosis	OR	P value	Confidence Interval
Unadjusted Odds	2.95068	0.000	2.683 - 3.244
Adjusted Odds for Age, Sex, Race and household income	2.67347	0.000	2.4255 2.9504
Additional adjustment for coexisting diagnosis of smoking, cocaine use, uncontrolled hypertension, diabetes and Hyperlipidemia	2.749	0.000	2.485- 3.040

The association between admission diagnosis of ACS and co-existing diagnosis of cannabis use was found to be statistically significantly, after matching for potential confounders.

Table 4. association between admission diagnosis of ventricular fibrillation and documented diagnosis of cannabis use disorder (Age 18-45).

Association between vfib admissions and cannabis use disorder diagnosis	OR	P value	Confidence Interval
Unadjusted Odds	2.713	0.000	1.809- 4.069
Adjusted Odds for Age, Sex, Race and household income	2.561	0.000	1.873 - 3.876
Additional adjustment for coexisting diagnosis of smoking, cocaine use, uncontrolled hypertension, diabetes and Hyperlipidemia	2.2974	0.000	1.5103 -3.493

The association between admission diagnosis of Ventricular fibrillation and co-existing diagnosis of cannabis use was found to be statistically significantly, after matching for potential confounders.

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Table 5. Analysis was done in the population selected based on diagnosis of cannabis use disorder. Analysis of comorbid conditions and their associations with acs as the admitting diagnosis: analysis done among admissions with documented diagnosis of cannabis use disorder : (age 18 -45).

CHARACTERISTICS OF ADMISSIONS WITH CANNABIS USE DISORDER	ASSOCIATION WITH ACS AS ADMISSION DIAGNOSIS: UNADJUSTED ODDS RATIO	ASSOCIATION WITH ACS AS ADMISSION DIAGNOSIS: ADJUSTED ODDS RATIO
Admissions with Black as the documented race	**1.73848 (1.4428 - 2.09711)** p value 0.000	**1.73522 (1.4391- 2.0935)** p value 0.000
Admissions with diagnosis of uncontrolled hypertension	**4.082651 (3.3829 - 4.927039)** P value 0.00	**4.08102 (3.37617 - 4.9185)** p value 0.000
Admissions with diagnosis of diabetes	**2.45692 (1.8591 - 3.24958)** P value 0.000	**2.37651 (1.8532 - 3.2458)** P value 0.000
Admissions with diagnosis of smoking	**1.5346 (0.04912 - 4.7935)** P value 0.000	
Admissions with diagnosis of cocaine use	**1.3361 (0.097481 - 1.82455)** P value 0.000	

Odds ratio was adjusted for age, sex, household income in probit logistic regression. Among the population of admissions with documented diagnosis of cannabis use disorder (age 18 - 45), those admissions with documented black race, uncontrolled hypertension and diabetes had statistically significant association with ACS as the admitting diagnosis. Co diagnosis of smoking or cocaine use did not reach statistical significance.

Propensity score and nearest neighbor matching and analysis among acs admissions in young adults.

Since the total number of acs admissions in young adults was much higher than compared to the subpopulation with cannabis use disorder, to analyze the in-hospital outcomes of acs, namely all-cause mortality, requirement of IABP, mean length of stay and mean of total charges, propensity score matched samples from the main sample were selected.

Propensity score and nearest neighbor matching (caliper width 0.2) was done among the acs admissions in young adults: exact matching was done for Age, Sex, Race, Income, Prevalence of smoking and cocaine use: each cohort had 380 subjects, differing only in cannabis use (CUD + and CUD - cohorts): outcomes of all-cause mortality, mean length of stay, total charges and requirement of intra-aortic balloon pump (IABP) during the admission was studied. (*Overall balance test- Hansen and Bowers: chi square 2.52, dF 6.00), using the relative multivariate imbalance (Lacus, king and porro 2010) had .161 after matching): no covariates exhibited a large imbalance > .25). SPSS 29 and R 4.3 were used to create the propensity score matched cohorts.*

	CUD + cohort	CUD - cohort
Total cohort size	**380**	**380**
Mean Age	**38.8236**	**38.8236**

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Sex	**Male**	**74.73%**	**Male**	**74.73%**
	Female	**25.26%**	**Female**	**25.26%**
Race	**Whites**	**43.68%**	**Whites**	**43.68%**
	Blacks	**40.23%**	**Blacks**	**40.23%**
	Hispanics	**13.94%**	**Hispanics**	**13.94%**
Quarterly Income	**1st quartile**	**45.51%**	**1st quartile**	**45.51%**
	2nd quartile	**23.42%**	**2nd quartile**	**23.42%**
	3rd quartile	**19.73%**	**3rd quartile**	**19.73%**
	4th quartile	**11.31%**	**4th quartile**	**11.31%**
Proportion of smokers	**0.005263**		**0.005263**	
Proportion of cocaine	**0.03157**		**0.03157**	
Proportion of all-cause mortality	**0.0078497**		**0.0078497**	
Proportion of patients requiring IABP	**2.10526%**		**1.57895%**	
Mean Length of stay (days)	**3.281579**		**2.6947**	
Mean of total hospital charges	**92390.64**		**908865.44**	

The requirement of IABP during the admissions, mean length of hospital stay and mean of total charges were higher in the cohort with cannabis use disorder among acs admissions, when compared to the cohort without cannabis use. No difference in all-cause mortality was seen between the two cohorts.

4. Discussion

As far as we know, this is the largest population-based analysis to date examining CUD+ and ACS/V. Fib admissions in the young adult population.

In this retrospective analysis, we found a highly significant odds ratio between cannabis users ages 18-44 and ACS-related admissions. This odds ratio remained highly significant even after running logistic regression models accounting for demographics (race, sex, age, socioeconomic status), comorbid conditions, cocaine use, marijuana use, etc. (OR 2.95, aOR 2.749). A previous retrospective NIS analysis including ages 11-70 demonstrated a significant odds ratio at 1.041 for acute-MI and cannabis use disorder after adjusting for confounders [10]. After similar adjustments were made in our analysis, the odds ratio for CUD+ and ACS was even more significant at 2.749 when looking only at ages 18-44. These odds imply stronger association between cannabis use and ACS admissions and younger adults. This may be due to stronger associations of confounders such as

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diabetes, hypertension, etc. in older adults, again suggesting that cannabis use has a more significant role in younger populations with precipitating ACS.

In the ACS and CUD+ group, there were higher percentages of males (73.64% vs. 66.93%), blacks (40.93% vs 22.54%), 1st quartile income (45.6% vs. 35.57%) and Medicaid recipients (39.52% vs. 27.88%). Further analysis revealed significant higher odds of blacks with CUD+ and ACS admissions, confirming our initial sample findings. Similar findings have been previously documented [12].

To further delineate in-hospital outcomes in ACS admissions with cannabis use, we used propensity score analysis with exact matching to compare all-cause mortality, requirement of IABP, mean length of stay and mean of total charges between CUD+ and CUD- patients. Patients in the ACS and CUD+ group had more IABP requirements (2.10% vs 1.58%), longer length of stay (~3.3 vs. ~2.7 days), and subsequent higher average hospital costs ($92,340 vs. $90,864).

Some studies have provided insight into what may be the cause of these significant trends. In one case-crossover study, the risk of myocardial infarction onset was elevated 4.8 times over baseline within the first 60 minutes of marijuana use, suggesting that it may be a rare trigger of MI [13]. One proposed mechanism is that CB1 receptors, a receptor in the human body that plays a protective role in myocardial ischemia and implicated to modulate chemotaxis, can be overactivated with exogenous delta-9-tetrahydrocannabinol (THC) consumption. In turn, inflammatory molecules are increased in the body promoting endothelial dysfunction and subsequent exacerbation of atherosclerosis [14].

Other studies discuss how smoking marijuana facilitates carboxyhemoglobin via combustion as well as upregulating sympathetic response [15,17]. This sympathetic response primarily manifests as tachycardia as cannabis increases sinus node automaticity via b-adrenergic stimulation [16,17]. Increased tachycardia coupled with possible decreased cellular oxygenation may provide the perfect storm for myocardial supply-demand mismatch, thereby inducing a type II myocardial infarction. There have also been animal models demonstrating larger atherosclerotic plaques compared to control when injected with THC comparable to one joint [14].

V. Fib association: Our analysis also looked at CUD+ and Ventricular fibrillation hospital admissions. Unadjusted odds were statistically significant at 2.713, however after adjusting for demographics and comorbidities the odds remained significant at 2.29. This correlates with previously documented findings, in which a sample population who underwent ambulatory Zio patch monitoring had a higher burden of arrhythmias with current Cannabis use [18]. As mentioned prior, this may be driven by the acute sympathetic changes that cannabis causes [17].

Limitations

One of the limitations with utilizing the national inpatient sample (NIS) is the inability to further evaluate CUD+ patients with amount using or duration of use. Over/under-reporting is also possible if there are ICD-10 coding errors in a database such as NIS. Additionally, while there is a significant adjusted odds ratio, no clear causation can be drawn from the data itself given the nature of the study, which would require more prospective/ randomized controlled trials.

Supplementary Materials: The following supporting information can be downloaded at the website of this paper posted on Preprints.org, Figure S1: title; Table S1: title; Video S1: title.

Funding: Research received no external funding.

Institutional Review Board Statement: study was done using NIS: retrospective study model: no IRB consent was required.

Informed Consent Statement: Not applicable.

Data Availability Statement: All analysis was done using National In-patient sample data for the year 2019.

Conflicts of Interest: Not applicable.

 doi:10.20944/preprints202404.2013.v1

References

1. Marijuana Use Among Young Adults (18–44 Years of Age) and Risk of Stroke | Stroke (ahajournals.org)
2. Marijuana and hallucinogen use among young adults reached all-time high in 2021 | National Institutes of Health (NIH)
3. Kicman A., Toczek M. The effects of Cannabidiol, non-intoxicating compound of cannabis, on the cardiovascular system in health and disease
4. Fong, H.k. Alarming trends in the frequency of malignant hypertension among admissions with a known cannabis use disorder
5. Desai, R. Hypertensive Crisis-related hospitalization and subsequent major adverse cardiac events in Young Adults with Cannabis USe Disorder: A Nationwide Analysis.
6. Marijuana Use, Diet, Body Mass Index, and Cardiovascular Risk Factors (from the CARDIA Study) - ScienceDirect
7. The function of the endocannabinoid system in the pancreatic islet and its implications on metabolic syndrome and diabetes
8. Chronic Marijuana Use Moderates the Correlations of Serum Cholesterol with Systemic Mitochondrial Function and Fluid Cognition - PMC (nih.gov)
9. Association of Cannabis Use With Cardiovascular Outcomes Among US Adults | Journal of the American Heart Association (ahajournals.org)
10. 1612427535-1612427529-20210204-18268-1ukzwb8.pdf (cureus.com)
11. Ventricular fibrillation triggered by marijuana use in a patient with ischemic cardiomyopathy: a case report | Cases Journal (springer.com)
12. Results from the 2013 National Survey on Drug Use and Health: Summary of National Findings (samhsa.gov)
13. Triggering Myocardial Infarction by Marijuana | Circulation (ahajournals.org)
14. Marijuana linked to heart disease; supplement may mitigate risk, study reports | News Center | Stanford Medicine
15. Latif Z, Garg N. The Impact of Marijuana on the Cardiovascular System: A Review of the Most Common Cardiovascular Events Associated with Marijuana Use. J Clin Med. 2020 Jun 19;9(6):1925. doi: 10.3390/jcm9061925. PMID: 32575540; PMCID: PMC7355963.
16. Ronald H. Miller, Ramesh C. Dhingra, Charles Kanakis, Fernando Amat-y-Leon, Kenneth M. Rosen, The electrophysiological effects of delta-9-tetrahydrocannabinol (cannabis) on cardiac conduction in man,American Heart Journal, Volume 94, Issue 6,1977,Pages 740-747, ISSN 0002-8703, https://doi.org/10.1016/S0002-8703(77)80215-9.
17. Malinowska B, Baranowska-Kuczko M, Schlicker E. Triphasic blood pressure responses to cannabinoids: do we understand the mechanism? Br J Pharmacol. 2012 Apr;165(7):2073-88. doi: 10.1111/j.1476-5381.2011.01747.x. PMID: 22022923; PMCID: PMC3413845.
18. Self-reported marijuana use and cardiac arrhythmias (from the Multiethnic Study of Atherosclerosis) - American Journal of Cardiology (ajconline.org)