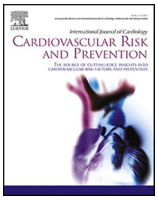
International Journal of Cardiology Cardiovascular Risk and Prevention 16 (2023) 200167

Contents lists available at ScienceDirect

International Journal of Cardiology Cardiovascular Risk and Prevention

journal homepage: www.journals.elsevier.com/international-journal-of-cardiology-cardiovascular-risk-and-prevention



Rising trend of acute myocardial infarction among young cannabis users: A 10-year nationwide gender and race stratified analysis

Harigopal Sandhyavenu [a,1], Harsh P. Patel [a,1], Riddhiben H. Patel [b], Rohan Desai [c], Achint A. Patel [d], Bhavin A. Patel [e], Jaimin Patel [f], Salman Zahid [g], Safi U. Khan [h], Abhishek Deshmukh [e], Khurram Nasir [h], Christopher V. DeSimone [e], Sourbha S. Dani [i], Samarthkumar Thakkar [h,*]

[a] Department of Internal Medicine, Louis A Weiss Memorial Hospital, Chicago, IL, USA
[b] Department of Internal Medicine, HCA Medical City Arlington, Dallas, Tx, USA
[c] Department of Internal Medicine, Texas Tech University Health Science Center El Paso, El Paso, Tx, USA
[d] Department of Public Health, Icahn School of Medicine Mount Sinai, New York, NY, USA
[e] Department of Cardiovascular Diseases, Mayo Clinic, Rochester, MN, USA
[f] Department of Internal Medicine, GCS Medical College, Gujarat, India
[g] Department of Internal Medicine, Rochester General Hospital, Rochester, NY, USA
[h] Department of Cardiovascular Medicine, Houston Methodist DeBakey Heart and Vascular Center, Houston, Tx, USA
[i] Department of Cardiology, Lahey Hospital & Medical Center, Burlington, MA, USA

ARTICLE INFO

Handling Editor: D Levy

Keywords:
Acute myocardial infarction
Young
Cannabis use
Black adults
Disparity

ABSTRACT

Background: The use of cannabis has massively increased among younger patients due to increasing legalization and availability.
Methods: We performed a retrospective nationwide study using the Nationwide inpatient sample (NIS) database to analyze the trends of acute myocardial infarction (AMI) in young cannabis users and related outcomes among patients aged 18–49 years from 2007 to 2018, using ICD-9 and ICD-10 codes.
Results: Out of 819,175 hospitalizations, 230,497 (28%) admissions reported using cannabis. There was a significantly higher number of males (78.08% vs. 71.58%, $p < 0.0001$) and African Americans (32.22% vs. 14.06%, $p < 0.0001$) admitted with AMI and reported cannabis use. The incidence of AMI among cannabis users consistently increased from 2.36% in 2007 to 6.55% in 2018. Similarly, the risk of AMI in cannabis users among all races increased, with the biggest increase in African Americans from 5.69% to 12.25%. In addition, the rate of AMI in cannabis users among both sexes showed an upward trend, from 2.63% to 7.17% in males and 1.62%–5.12% in females.
Conclusion: The incidence of AMI in young cannabis users has increased in recent years. The risk is higher among males and African Americans.

1. Introduction

The legalization of cannabis in United States for recreational purposes has led to increased consumption in young adults significantly more than in any other age group, which raises concerns over its safety and cardiovascular (CV) effects [1,2]. Evidence on the association between cannabis use and cerebrovascular and cardiovascular (CV) accidents is growing [3–7]. Hence, the American Heart Association (AHA) has recommended refraining from indulging in such products [8,9]. Cannabis consumption may lead to acute myocardial infarction (AMI) by altering the coronary blood flow and heart rate, increasing oxygen demand [10]. There is a lack of data on national trends and racial and demographic differences in young cannabis users hospitalized with AMI. The AHA has also identified the need for further research on the epidemiological trends of cannabis use in young adults and its association with AMI, further highlighting the need for increased research in

* Corresponding author. Department of Cardiovascular Disease, Houston Methodist DeBakey Heart and Vascular Center, 6565 Fannin St, Houston, TX, 77030, USA.
E-mail address: drthakkar.samarth@gmail.com (S. Thakkar).
[1] Drs. Sandhyavenu and Patel contributed equally to this manuscript as co-first authors.

https://doi.org/10.1016/j.ijcrp.2022.200167
Received 30 June 2022; Received in revised form 20 December 2022; Accepted 22 December 2022
Available online 29 December 2022

this area [8]. This study aimed to analyze the trends of AMI in young cannabis users and related in-hospital outcomes among patients aged 18–49 years, spanning from 2007 to 2018, further stratified by race and gender.

2. Methods

2.1. Data source

A retrospective analysis of 819,175 AMI hospitalizations of patients aged 18–49 years with or without cannabis use was performed from 2007 to 2018 using the National Inpatient Sample (NIS) database. The NIS is one of the largest family of databases developed by the Agency for Healthcare Research and Quality (AHRQ) for Healthcare Cost and Utilization Project (HCUP). The database includes hospitalizations of insured and uninsured patients in the US and is weighted; it estimates more than 35 million hospitalizations over 48 states across the nation. Its large sample size is ideal for developing national and regional estimates and enables the analysis of special populations. Data provided from NIS contains clinical and nonclinical data elements for each hospital stay while maintaining patient confidentiality by removing State and hospital identifiers. Data has been de-identified with prior ethical committee approval; therefore, no additional ethical committee approval was required for our analysis. We followed STROBE guidelines for observational studies as described in Supplementary Table 1.

2.2. Study cohort

International Classification of Diseases, 9th and 10th Revision, Clinical Modification (ICD-9 and 10- CM) codes were used to identify hospitalizations in patients aged 18–49 years with AMI with or without cannabis use. In addition, demographic details such as age, gender, race, comorbidities, median household income, insurance status, hospital characteristics, and regions were also studied.

2.3. Statistical analysis

As recommended, survey procedures using discharge weights provided with HCUP-NIS databases were used to generate national estimates. Descriptive statistics were used to analyze the demographic and comorbidity data. Most hospital-level characteristics were directly obtained as provided in the NIS, whereas the Elixhauser Comorbidity Index was used to identify comorbid disorders. Categorical variables were compared using the Chi-square test and are presented as numbers and percentages. Numerical variables were compared using the Wilcoxon test and are presented as the median and interquartile range (IQR). A two-tailed p-value of 0.05 was used to determine the statistical significance. We also performed multivariable logistic regression for predictors of AMI among young cannabis users. The Jonckheere-Terpstra trend test was used to analyze various trends. We utilized SAS 9.4 (SAS Institute, Inc, Cary, North Carolina) software for all statistical analyses.

3. Results

3.1. Baseline characteristics

There were 819,175 hospitalizations in patients from 18 to 49 years of age who suffered AMI between 2007 and 2018. Of these, 28% (230,497) of admissions reported using cannabis. (Fig. 1 and S1). AMI admissions with cannabis use had a higher proportion of males (78.08% vs. 71.58%, $p < 0.0001$) and African Americans (32.22% vs. 14.06%, $p < 0.0001$). Baseline comorbidities were significantly higher in non-cannabis users including obesity (23.23% vs 20.65%, $p < 0.0001$), hypertension (57.09% vs 55.1%, $p < 0.001$), diabetes mellitus (21.25% vs 13.42%, $p < 0.000$), and congestive heart failure (1.09% vs 0.8%, $p < 0.0001$) among others. Cannabis user groups reported a higher rate of

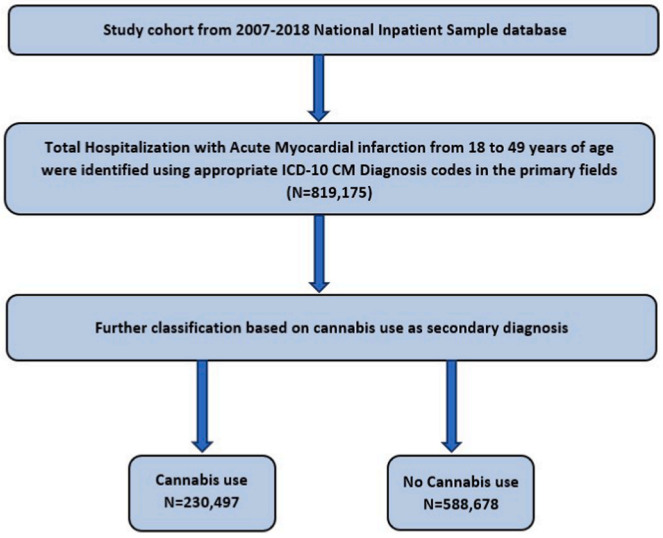


Fig. 1. The study population selection-algorithm.

alcoholism (16.88% vs. 4.63%, $p < 0.0001$) and drug abuse (80.28% vs. 4.91%, $p < 0.0001$) comparatively. The cannabis group had more patients with Medicare or Medicaid as primary insurance (42.52% vs. 28.28%, $p < 0.0001$) than non-cannabis with AMI (Table 1).

3.2. Temporal trends

Across the study period, the overall incidence of AMI in young cannabis users increased from 2.3% in 2007 to 6.5% in 2018 (Fig. 2). The youngest partition of the age range (18–34) had a higher rate of AMI than the latter age group (35–49); however, the trend of AMI increased among both age sub-groups (7.3%–13.9% and 1.95–5.88%, respectively) (Fig. 3). Furthermore, the percentage risk of AMI in young cannabis users was rising across all races, with the most significant increase in African Americans from 5.69% to 12.25% (Fig. 4). Finally, the rate of AMI in young cannabis users amongst both sexes increased as well, from 2.63% to 7.17% in males and 1.62%–5.12% in females (Fig. 5).

3.3. Predictors of MI

Multivariable logistic regression analysis identified the following independent predictors of MI; age (odds ratio (OR): 2.962, 95% confidence interval [CI]:2.753–3.187, p= <0.0001), male gender (OR: 1.532, 95% CI: 1.432–1.639, p= <0.0001), African American race (OR: 2.59, 95% CI: 2.43–2.77, p= <0.0001), alcoholism (OR: 2.92, 95% CI: 2.69–3.17, p= <0.0001), depression (OR: 1.19, 95% CI: 1.08–1.32, $p = 0.005$), psychosis (OR 1.76, 95% CI: 1.58–1.98, p= <0.0001) and smoking (OR: 2.38, 95% CI: 2.23–2.54, p= <0.0001) (Table 2).

4. Discussion

We report on a nationwide population-based study examining the association of cannabis use with AMI among young to middle-aged patients (18–50 years). The key findings of this analysis are the following: 1) A significant increase in the incidence of AMI among cannabis users; 2) Higher numbers in Males; 3) Higher numbers in African Americans, and 4) Higher numbers in younger vs. middle-aged users.

In this study, we found a significant increase in the incidence of AMI among cannabis users, with a higher trend observed in the younger age group between 18 and 34 years compared to 35–49 years. This is consistent with the Behavioral Risk Factor Surveillance System (BRFSS) data showing the highest consumption of cannabis among the 18–34

Table 1
Baseline Characteristics of study population.

Characteristics	No cannabis use N = 588,678	Cannabis use N = 230,497	p-value
Overall			
Age in years (mean ± SE)	43 ± .014	40 ± .084	
Age in years (%)			<0.0001
18–34	7.29	20.17	
35–49	92.71	79.83	
Gender (%)			<0.0001
Male	71.58	78.08	
Female	28.4	21.9	
Race (%)			<0.0001
White	58.58	47.67	
Black	14.06	32.22	
Hispanic	9.3	7.54	
Others	6.94	4.47	
Missing			
Comorbidities (%)			
Obesity	23.23	20.65	<0.0001
Hypertension	57.09	55.1	<0.0001
Diabetes mellitus	21.25	13.42	<0.0001
Congestive heart failure	1.09	0.8	<0.0001
Valvular heart disease	0.4	0.25	<0.0001
History of chronic pulmonary disease	11.45	13.9	<0.0001
Pulmonary circulatory disease	0.12	0.08	0.0257
Peripheral vascular disease	3.7	3.83	0.2295
Paralysis	0.79	1.06	<0.0001
Coagulopathy	2.65	2.95	0.001
Metastatic cancer	0.18	0.09	0.0002
Weightloss	0.99	1.12	0.0188
Liver disease	1.54	1.92	<0.0001
Alcoholism	4.63	16.88	<0.0001
Drug abuse	4.91	80.28	<0.0001
Median household income (%)			<0.0001
1st quartile	31.66	42.66	
2nd quartile	26.66	25.81	
3rd quartile	22.33	18.79	
4th quartile	17.01	10.29	
Primary Insurance (%)			<0.0001
Medicare/Medicaid	28.28	42.52	
Private including HMO	49.24	24.66	
Uninsured/Self-pay	22.28	32.62	
Hospital bed size (%)			<0.0001
Small	11.16	12.06	
Medium	25.52	27.19	
Large	62.83	60.2	
Hospital Type (%)			<0.0001
Rural	7.55	5.96	
Urban-Nonteaching	34.52	27.67	
Teaching	57.45	65.82	
Hospital region (%)			<0.0001
Northeast	16.37	14.35	
Midwest	23.36	25.7	
South	43.99	42.65	
West	16.28	17.3	
Day of admission			<0.0001
Weekday	72.8	71.08	
Weekend	27.2	28.92	
Source of admission (%)			<0.0001
Transfer from other hospital or other health facility	30.31	26.59	
Emergency department	69.69	73.41	
Type of admission (%)			<0.0001
Emergent or Urgent	94.09	96.06	
Elective	5.91	3.94	
Disposition status (%)			<0.0001
Home	88.53	90.29	
Facility	9.68	8.36	
Died	1.71	1.29	
Length of stay (LOS) (mean ± SE)	3.46 ± 0.01	3.27 ± 0.04	

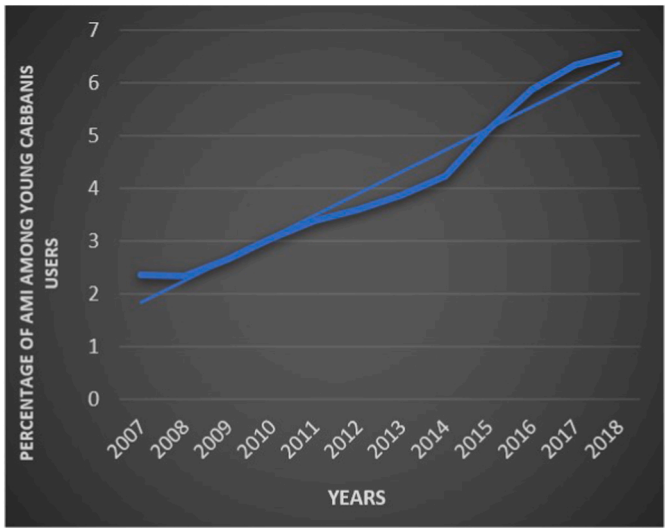


Fig. 2. Trend of AMI hospitalizations in young cannabis users.

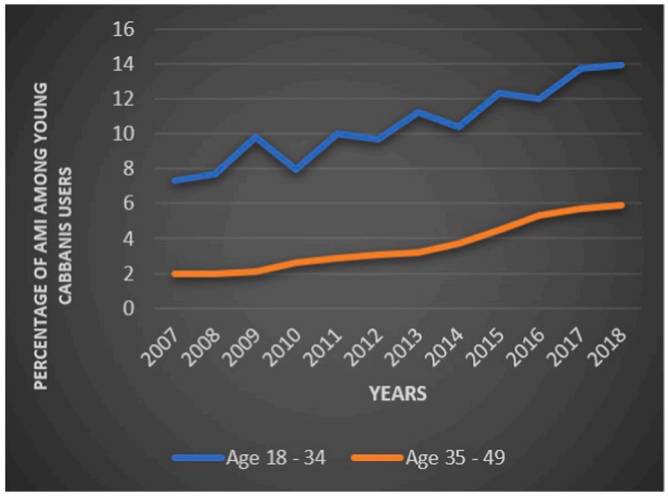


Fig. 3. Trend of AMI hospitalizations in young cannabis users according to age group.

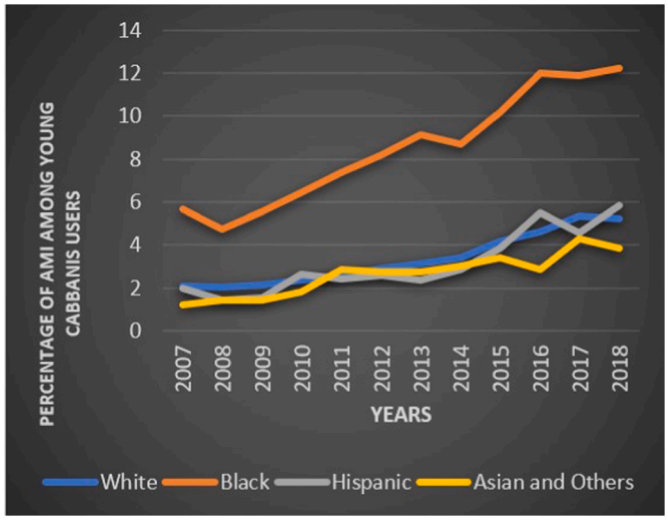


Fig. 4. Trend of AMI hospitalizations in young cannabis users according to ethnicity.

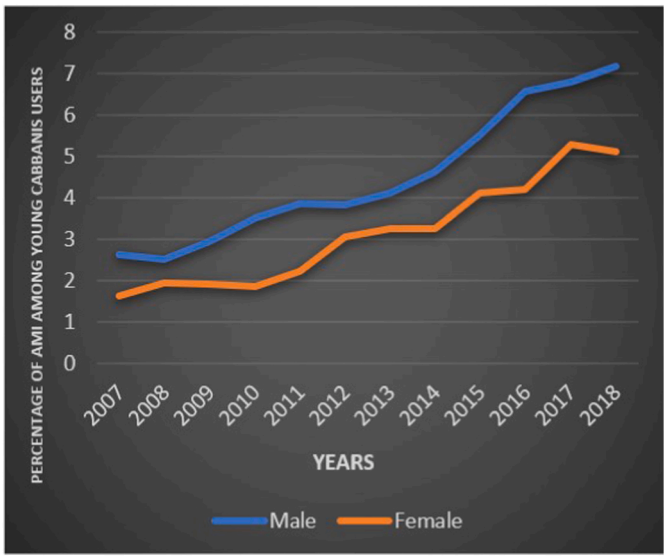


Fig. 5. Trend of AMI hospitalizations in young cannabis users according to gender.

Table 2
Predictors of AMI in young cannabis users.

Independent variable/Characteristic	OR	LL	UL	P
Year	1.118	1.106	1.13	<0.0001
Age (10 years increase)	2.962	2.753	3.187	<0.0001
Gender (%)				
Male	1.532	1.432	1.639	<0.0001
Female	ref			
Race (%)				
White	ref			
Black	2.59	2.43	2.77	<.0001
Hispanic	0.88	0.79	0.99	0.03
Others	0.80	0.69	0.92	0.02
Comorbidity				
Obesity	0.85	0.796	0.907	<0.0001
Paralysis	0.946	0.718	1.246	0.6927
Neurological disease	1.14	0.99	1.32	0.05
Metastatic cancer	0.521	0.188	1.443	0.2096
Weight loss	0.94	0.72	1.23	0.68
Anemia	0.89	0.80	0.98	0.02
Alcoholism	2.92	2.69	3.17	<.0001
Depression	1.19	1.08	1.32	0.005
Smoking	2.38	2.23	2.54	<.0001
Median household income (%)				
1st quartile	1.27	1.15	1.41	<.0001
2nd quartile	1.12	1.01	1.25	0.02
3rd quartile	1.11	1.01	1.23	0.04
4th quartile	Ref			
Primary Insurance (%)				
Medicare/Medicaid	ref			
Private including HMO	0.47	0.44	0.51	<.0001
Uninsured/Self-pay	1.05	0.98	1.13	0.11
Admission Type				
Non elective	ref			
Elective	0.76	0.66	0.88	0.002

years age group compared to later [11]. Alongside the rising cannabis use, there are increased adverse cardiovascular outcomes such as MI, arrhythmias among young cannabis consumers [8]. We noticed a linear correlation between the rate of legalization of cannabis for medical and recreational purposes and the incidence of AMI among the young. By 2012, about 18 states legalized medical use of cannabis, and around the same time, Colorado and Washington became the first two states to legalize the recreational use of cannabis since then more numbers of states have approved both medical and recreational use of cannabis [12]. There is a geographic variation in the rates of AMI hospitalization in the United States among cannabis users in our study. The percentage of AMI was predominantly higher among cannabis users in the mid-western and western regions which could be attributable to the easy availability of cannabis products due to legalization in many states in these regions. Our study showed a consistently rising trend of AMI among young cannabis users from 2008, which got even steeper in 2014 onwards.

In our study, the overall incidence of AMI among cannabis users was higher in males, with a rising incidence in females. According to the 2018 National survey on drug use and health in Women, cannabis is the most used recreational drug in women, increasing the number of consumers from 12.5% to 13.4% between 2017 and 2018. A higher incidence of AMI in African American and lower household income groups was another study finding reported consistently across the literature [5,7,12,13]. African American adults, in general, have been found to have a higher rate of cannabis use disorders, along with other cardiac comorbidities like hypertension, hyperlipidemia, and increased concomitant use of other illicit substances, all of which could be contributory [14,15]. Economic challenges, increased psychosocial problems, including relationship conflicts, workspace problems, depression, and psychosis, with low access to cannabis cessation program make them more vulnerable to substance use disorder and a myriad of health problems [15,16].

Interestingly, the prevalence of major cardiac comorbidities like obesity, hypertension, diabetes mellitus, and congestive heart failure was significantly lower in the cannabis user group than among nonusers. Despite these traditionally significant risk factors for AMI, the cannabis use group had lower rates of comorbidities but higher rates of AMI. This finding emphasizes cannabis use as an independent risk factor for acute coronary events. The biological effects of cannabis on the cardiovascular system are complex and less studied [17]. Several theories have been postulated: increase in carboxyhemoglobin hence decrease in oxygen-carrying capacity, increase in factor VII activity leading to hypercoagulability, direct vasculotoxic effects, increased sympathetic activation, all resulting in mismatch oxygen demand and supply [18,19]. It has been hypothesized that it can cause direct hemodynamic stress leading to atherosclerotic plaque disruption and acute occlusive thrombus, but a dose frequency relationship to these biochemical events has not been established yet [20,21].

Although the incidence of AMI was higher among cannabis users independent of dosage and mode consumed, the overall mortality was lower than for nonusers [5,22]. The lower odds of mortality among cannabis users with AMI could be explained by the lower prevalence of other cardiac comorbidities. Furthermore, it is interesting to note that apart from alcoholism and smoking, the presence of depression or psychosis was found to be an independent predictor of AMI in cannabis users.

4.1. Limitations

This study has its limitations which should be considered while interpreting results due to the inherent nature of national databases. For example, although we have utilized previously validated ICD codes, we cannot exclude some administrative coding errors resulting in over-reporting or under-reporting. In addition, there can be a possibility of reporting bias as the study population is young and more likely to under-report due to the reluctance or fear of social stigma. Furthermore, the database does not have follow-up data to gauge morbidity and mortality after discharge. Finally, since the consumption mode, dosage, and time to exposure were unknown, we could only measure lifetime association with AMI. We also cannot determine the granularity of drug use type and amount per user, especially in addition to cannabis use.

5. Conclusion

This hypothesis-generating data highlight a concerning trend of

increased AMI among young cannabis users. In addition, the increase is more exaggerated in males, African Americans, and low-income status. These data support that cannabis may be an independent risk factor for AMI. The medical community should remain prudent about the health hazards of consuming cannabis and increase awareness in high-risk populations. These data merit further evaluation in the prospective cohort analysis.

Credit author

Harigopal Sandhyavenu: Conceptualization, Methodology, Data Collection, Writing – Original draft, Writing – Review & editing. **Harsh P Patel:** Conceptualization, Methodology, Software, Formal analysis, Writing – Original draft, Writing – Review & editing. **Riddhiben H Patel:** Writing – Original draft, Writing – Review & editing. **Rohan Desai:** Writing – Original draft, Data Collection, Writing – Review & editing. **Achint A. Patel:** Writing – Original draft, Writing – Review & editing. **Bhavin A. Patel:** Writing – Original draft, Writing – Review & editing. **Jaimin Patel:** Writing – Original draft, Writing – Review & editing. **Salman Zahid:** Writing – Original draft, Writing – Review & editing. **Safi U Khan:** Writing – Original draft, Writing – Review & editing. **Abhishek Deshmukh:** Writing – Original draft, Writing – Review & editing, Supervision. **Khurram Nasir:** Writing – Original draft, Writing – Review & editing, Supervision. **Christopher V. DeSimone:** Writing – Original draft, Writing – Review & editing, Supervision. **Sourbha S Dani:** Writing – Original draft, Writing – Review & editing, Supervision. **Samarthkumar Thakkar:** Conceptualization, Writing – Original draft, Writing – Review & editing, Supervision.

Funding

None.

Disclosures, conflict of interests and acknowledgement

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcrp.2022.200167.

References

[1] H. Goyal, H.H. Awad, J.K. Ghali, Role of cannabis in cardiovascular disorders, J. Thorac. Dis. 9 (7) (2017) 2079–2092.
[2] M. Cerdá, A.L. Sarvet, M. Wall, T. Feng, K.M. Keyes, S. Galea, et al., Medical marijuana laws and adolescent use of marijuana and other substances: alcohol, cigarettes, prescription drugs, and other illicit drugs, Drug Alcohol Depend. 183 (2018) 62–68.
[3] M.A. Mittleman, R.A. Lewis, M. Maclure, J.B. Sherwood, J.E. Muller, Triggering myocardial infarction by marijuana, Circulation 103 (23) (2001) 2805–2809.
[4] T. Chami, C.H. Kim, Cannabis abuse and elevated risk of myocardial infarction in the young: a population-based study, Mayo Clin. Proc. 94 (8) (2019) 1647–1649.
[5] R. Desai, H.K. Fong, K. Shah, V.P. Kaur, S. Savani, K. Gangani, et al., Rising trends in hospitalizations for cardiovascular events among young cannabis users (18–39 years) without other substance abuse, Medicina 55 (8) (2019) 438.
[6] C.P. Johnson-Sasso, C. Tompkins, D.P. Kao, L.A. Walker, Marijuana use and short-term outcomes in patients hospitalized for acute myocardial infarction, PLoS One 13 (7) (2018).
[7] R.S. Patel, S.R. Katta, R. Patel, V. Ravat, R. Gudipalli, V. Patel, et al., Cannabis use disorder in young adults with acute myocardial infarction: trend inpatient study from 2010 to 2014 in the United States, Cureus 10 (8) (2018), e3241.
[8] R.L. Page, L.A. Allen, R.A. Kloner, C.R. Carriker, C. Martel, A.A. Morris, et al., Medical marijuana, recreational cannabis, and cardiovascular health: a scientific statement from the American heart association, Circulation 142 (10) (2020).
[9] T. Parekh, S. Pemmasani, R. Desai, Marijuana use among young adults (18–44 years of age) and risk of stroke, Stroke 51 (1) (2020) 308–310.
[10] G. Thomas, R.A. Kloner, S. Rezkalla, Adverse cardiovascular, cerebrovascular, and peripheral vascular effects of marijuana inhalation: what cardiologists need to know, Am. J. Cardiol. 113 (1) (2014) 187–190.
[11] Behavioral Risk Factor Surveillance System (BRFSS) data | Monitoring health concerns related to marijuana. Accessed April 12, 2022. https://marijuanahealthinfo.colorado.gov/health-data/behavioral-risk-factor-surveillance-system-brfss-data.
[12] States where recreational marijuana is legal - ProCon.org. Accessed April 12, 2022. https://marijuana.procon.org/legal-recreational-marijuana-states-and-dc/.
[13] R. Desai, S. Shamim, K. Patel, A. Sadolikar, V.P. Kaur, S. Bhivandkar, et al., Primary causes of hospitalizations and procedures, predictors of in-hospital mortality, and trends in cardiovascular and cerebrovascular events among recreational marijuana users: a five-year nationwide inpatient assessment in the United States, Cureus 10 (8) (2018), e3195.
[14] G.A. Mensah, Cardiovascular diseases in African Americans: fostering community partnerships to stem the tide, Am. J. Kidney Dis. 72 (5) (2018).
[15] L.T. Montgomery, C. Robinson, E.L. Seaman, A.M. Haeny, A scoping review and meta-analysis of psychosocial and pharmacological treatments for cannabis and tobacco use among African Americans, Psychol. Addict. Behav. 31 (8) (2017) 922–943.
[16] S. Cobb, M. Bazargan, J. Smith, H.E. del Pino, K. Dorrah, S. Assari, Marijuana use among African American older adults in economically challenged areas of South Los Angeles, Brain Sci. 9 (7) (2019) 166.
[17] M.R. Piano, Cannabis smoking and Cardiovascular Health: it's complicated, Clin. Pharmacol. Therapeut. 102 (2) (2017) 191–193.
[18] C.H. Ashton, Pharmacology and effects of cannabis: a brief review, Br. J. Psychiatry 178 (2) (2001) 101–106.
[19] W.S. Aronow, J. Cassidy, Effect of marihuana and placebo-marihuana smoking on angina pectoris, N. Engl. J. Med. 291 (2) (1974) 65–67.
[20] J.E. Muller, G.H. Tofler, P.H. Stone, Circadian variation and triggers of onset of acute cardiovascular disease, Circulation 79 (4) (1989) 733–743.
[21] J.E. Muller, G.S. Abela, R.W. Nesto, G.H. Tofler, Triggers, acute risk factors and vulnerable plaques: the lexicon of a new frontier, J. Am. Coll. Cardiol. 23 (3) (1994) 809–813.
[22] R. Desai, U. Patel, S. Sharma, P. Amin, R. Bhuva, M.S. Patel, et al., Recreational marijuana use and acute myocardial infarction: insights from nationwide inpatient sample in the United States, Cureus 9 (11) (2017), e1816.