When Cannabis Use Goes Wrong: An Epidemiologic Study of Cardiopulmonary Symptoms in Patients That Present to Emergency Departments

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Background: *Increased availability and use of cannabis in Michigan have led to a marked increase in emergency department (ED) visits associated with the drug's adverse cardiopulmonary effects. However, few people are aware of these potential cardiopulmonary side effects. Recognition of these presenting symptoms is critical for emergency clinicians to provide timely and effective care, make accurate diagnoses, and safeguard the health of patients who may be experiencing toxic effects from cannabis use.*
Study objective: *To describe the prevalence, clinical features, and disposition of cannabis cardiopulmonary toxicity in a community-based study.*
Methods: *This was a retrospective cohort analysis of all patients diagnosed with toxicity related to cannabis use. Patients were seen at eight EDs over a 26-month study period (November 2018–December 2020). Affiliated institutions included three university-affiliated hospitals, a children's tertiary care facility, and four rural medical centers. Data collected included demographics, clinical features, and treatment outcomes in patients presenting to the ED with cardiopulmonary symptoms (CPS) versus those experiencing other forms of cannabis toxicity.*
Results: *During the study period, 1,174 patients were evaluated for cannabis toxicity. A total of 318 patients (27.1%) had a cardiopulmonary chief complaint (CPS group) and 856 (72.9%) experienced other forms of cannabis toxicity, predominantly symptoms of intoxication, cannabis hyperemesis syndrome, or neuropsychiatric complaints. The CPS group presented with tachycardia (36.5%), dyspnea (34.3%), chest tightness (28.6%), palpitations (17.9%), and hypertension (8.2%). CPS patients were more likely to be older (32.6 vs. 24.3 years, $p < 0.001$), ingested edible cannabis (36.8% vs. 9.2%, $p < 0.001$), and have a history of polysubstance abuse (17.6 vs. 12.0%, $p = 0.013$). These patients also had a longer ED length of stay (4.9 vs. 3.8 h, $p < 0.001$) and significantly more hospital admissions (10.1% vs. 6.3%, $p = 0.027$).*
Conclusions: *Cardiopulmonary toxicity is common after acute or chronic cannabis exposures, occurring in over one-quarter of ED patients in this community-based study. These troublesome findings highlight the risks associated with using cannabis for recreational or therapeutic purposes.*

Keywords: *cannabis; toxicity; cardiopulmonary; clinical features*

INTRODUCTION

Cannabis is one of the most used recreational drugs, with estimates that 147 million people used the drug in 2019, about 2.5% of the global population.[1] This number continues to climb owing to low prices, increased legalization, and the perception that cannabis has less potential for abuse than alcohol and other illicit recreational drugs. In 2018 Michigan became the first state in the Midwest to approve the recreational use of cannabis, ending a decade-long debate over legalization. Since this law was enacted, increased availability and use of cannabis have led to increased hospitalizations and emergency department (ED) visits due to cannabis toxicity.[2] Until recently, the effects of cannabis on other organ systems beyond the psychiatric and hallucinogenic effects have not been largely investigated. There have been some reports suggesting an association between cannabis use and a wide range of effects on the pulmonary and cardiovascular systems. These adverse effects include myocardial ischemia, arrhythmias, cardiomyopathies, sudden cardiac death, arteritis, blood pressure changes, peripheral vascular

complications, and acute or chronic lung disease among others.[3–12] One review summarized the three main cardio-pulmonary pathologies associated with cannabis use: coronary vasospasms, peripheral arteritis, and platelet aggregation. However, many of the acute and, more so, long-term potentially toxic effects of cannabis and 9-tetrahydrocannabinol (THC) still remain unknown.[13] Despite these reports, the public is generally unaware of these potential cardiopulmonary side effects. The legalization of cannabis possession and the spread of information regarding the potential therapeutic qualities of medicinal cannabinoids have led to the perception of cannabis as a harmless (or even 'beneficial') substance.[14] Yet, cannabis is increasingly recognized as a potential underlying cause of cardiopulmonary emergencies in patients without other risk factors.

This is one of the few epidemiologic studies in the United States to examine cardiopulmonary symptoms (CPS) secondary to cannabis toxicity in patients presenting to EDs. Awareness of these presenting symptoms is critical for emergency clinicians to provide timely and effective care, make accurate diagnoses, and safeguard the health of patients who may be experiencing adverse effects from cannabis use. To achieve this goal, we specifically examined the prevalence, clinical features, and outcomes of patients displaying CPSs related to cannabis consumption.

METHODS

Study Design

We conducted a retrospective chart review of all ED patients diagnosed with cannabis toxicity over a 26-month study period. Spanning 13 counties in Michigan, affiliated institutions included four rural medical centers, three university-affiliated hospitals, and a children's tertiary care facility. The study was approved by the institutional review board (IRB) at Corewell Health (2019-353).

Study Population

All ED patients were seen at participating hospitals from November 2018 to December 2020 with a primary diagnosis of acute cannabis-related disorders/poisoning. If a patient had more than one visit to any hospital during the study period, all visits were included for review. Patients were identified using the data acquisition services of our institution's research scientific support team with the following ICD-10 codes used in the main diagnostic field: F12 (cannabis-related disorders) or T40.7 (cannabis poisoning). Patients were excluded if they had missing data or incomplete documentation.

Data Collection and Validation

All data were collected by medical students and residents with training in research methodology and blinded to the study objectives. Research staff were trained in data by faculty abstraction using a set of mock case records. Data abstraction was reviewed regularly by the research staff. Abstracted data included demographics, clinical findings, and treatment outcomes in patients presenting with CPS. This population was compared to ED patients experiencing other forms of cannabis toxicity. For the purposes of this study, acute cannabis intoxication was defined as perception alterations, mild motor impairment, euphoria, and intensification of ordinary sensory experiences.[2,5]

Statistical Analyses

The primary outcome measures were the frequency and type of CPSs documented in ED patients with cannabis toxicity. To account for potential COVID-19 pandemic influences on ED visits, a post-hoc subset analysis was conducted on patients presenting before and during the first 9 months of the pandemic (March 2020–December 2020). Data were entered into a Microsoft Excel database (Microsoft Corp, Redmond, WA, USA). All analyses were performed using SAS statistical software version 9.4 (SAS Institute, Cary, NC, USA). One investigator performed a blinded critical review of a random sample of 10% of the medical records to determine the inter-rater reliability of data collection using the Kappa reliability test.[15] Descriptive statistics were described as means, standard deviation, and frequency distributions. T-tests and chi-squared tests were used to compare key demographic and outcome variables between our two patient groups: those with cardiopulmonary chief complaints (CPS) and other forms of cannabis toxicity.

RESULTS

During the 26-month study period, 1,174 patients were evaluated for cannabis toxicity. A total of 318 patients (27.1%) had a cardiopulmonary chief complaint (CPS group), and 856 (72.9%) experienced other forms of cannabis toxicity. The mean age was 26.5 + 9.1 years (range, 6 mos-84). Ninety-two patients (7.8%) were >64 years old, and 34 (2.9%) were children <12 years of age. One hundred thirty-one (11.2%) arrived by emergency

medical services (EMS), with 56 requiring prehospital treatment (naloxone, oxygen). Polysubstance use was reported in histories and/or drug screens in 159 (13.5%), with the most common substances being ethanol and cocaine.

The CPS group commonly presented with tachycardia, severe dyspnea, chest tightness, and palpitations (Table 1). In comparison, patients experiencing other forms of cannabis toxicity presented predominantly with symptoms of intoxication, cannabis hyperemesis syndrome, or neuropsychiatric symptoms. Many patients in our comparison group also had mild CPSs such as cough, dyspnea, and palpitations. Patients in the CPS group were more likely to be older, consumed an edible form of cannabis, and had a history of polysubstance abuse (Table 2). These patients also had more extensive workups and a longer ED length of stay (4.9 vs. 3.8 h). Hospital admissions in the CPS group were generally related to preexisting comorbidities; three patients were diagnosed with hypertensive urgency. Fourteen

Table 1. Presenting complaints in CPS patients versus those experiencing other forms of cannabis toxicity.

CPS (*N* = 318)		Other Forms of Cannabis Toxicity (*N* = 856)	
Tachycardia	116 (36.5%)	Intoxication*	439 (51.3%)
Dyspnea	109 (34.3%)	Nausea/vomiting, abdominal pain	390 (45.6%)
Chest tightness	91 (28.6%)	Anxiety, panic attack	390 (45.6%)
Palpitations	57 (17.9%)	Agitation/aggression	99 (11.6%)
Cough	33 (10.4%)	Paranoia, hallucinations	79 (9.2%)
Hypertension	26 (8.2%)	Suicidal ideation, depression	67 (7.8%)
Diaphoresis	19 (6.0%)	Blurry vision, HA, tremulous, dizziness	46 (5.4%)
Syncope	12 (3.8%)	Miscellaneous‡	45 (5.3%)
Wheezing	11 (3.5%)		
Tachypnea	11 (3.5%)		
Hypotension	7 (2.2%)		

*Cannabis intoxication was defined as euphoria, perception alterations such as time and spatial distortion, mild motor impairment, and intensification of ordinary sensory experiences.
‡Miscellaneous included sore throat, dry mucous membranes, flushing, hypothermic, myalgia, fatigue, amnesia and seizures.

Table 2. Patient demographics and outcomes.

	CPS Patients (*N* = 318)	Other Forms of Cannabis Toxicity (*N* = 856)	*p*
Mean age (SD)	32.6 + 15.8 yrs	24.3 + 12.4 yrs	<0.001
Gender (% female)	144 (45.3%)	400 (46.7%)	0.669
Race (% white)	181 (56.9%)	493 (57.6%)	0.829
Duration of symptoms (h)	14.7 + 22.6	20.1 + 20.0	<0.001
Edible cannabis	117 (36.8%)	79 (9.2%)	<0.001
History of cardiopulmonary disease	36 (11.3%)	77 (9.0%)	0.235
Other comorbidities*	102 (32.1%)	286 (33.4%)	0.674
History of polysubstance abuse	56 (17.6%)	103 (12.0%)	0.013
Emergency department LOS (h)‡	4.9 + 3.9	3.8 + 2.6	<0.001
Outcomes			
Admitted	32 (10.1%)	54 (6.3%)	0.027
Transfer (psychiatric)	5 (1.6%)	46 (5.4%)	0.005
Jail	2 (0.6%)	15 (1.8%)	0.130
Self-discharge	2 (0.6%)	11 (1.3%)	0.309

*Comorbidities include diabetes, cancer, chronic kidney disease, mental and behavioral disorders, peripheral vascular disease, cerebrovascular disease, epilepsy, dementia, and inflammatory bowel disease.
‡LOS defined as length of stay in the emergency department.

patients had frequent premature ventricular contractions (PVCs), but no ischemic events, unstable angina, or serious tachyarrhythmias. The reliability of data collection ($k = 0.89$) showed excellent agreement.

A subset analysis was conducted on patients presenting before and during the first 9 months of the pandemic (March 2020–December 2020). During this 9-month period, ED visits attributable to cannabis use decreased by 9.3% (4.2 patients/month). However, the prevalence of cardiopulmonary chief complaints among cannabis users presenting during the pandemic remained unchanged (27.5% vs. 26.9%, $p = 0.830$). Clinical features and outcomes of patients displaying CPSs before and during the first 9 months of the pandemic were also not significantly different.

DISCUSSION

In this retrospective analysis in eight EDs in West Michigan, cardiopulmonary toxicity was common after acute or chronic cannabis exposures, occurring in over one-quarter of patients. This prevalence and spectrum of cardiopulmonary adverse events aligns with a prior study of clinical presentations related to acute cannabis toxicity from Switzerland[6] and a study from the European Drug Emergencies Network, which used data from 36 centers in 24 European countries.[7] A retrospective study of 8,598 cannabis-intoxicated adult patients who presented at an Amsterdam inner-city ED found that 47.2% reported cardiovascular symptoms.[16] Palpitations were most common complaint, followed by syncope and chest pain. Eight patients (0.5%) had cardiovascular complications including atrial fibrillation, myocardial infarction, and AV-nodal reentrant tachycardia. No epidemiologic studies have been performed in the United States specifically examining CPSs in ED patients. However, a study in Kentucky used administrative billing data for ED visits to characterize 1,490 cases of cannabis toxicity.[17]

Severe cardiac complications occurred in nearly a fifth of people diagnosed with cannabinoid poisoning including hypertensive heart disease, hypertensive crisis, paroxysmal tachycardia, or hypotension. Roughly a third of all these events involved combined toxicity with another psychoactive substance, primarily stimulants and opioids.[17] Although the clinical significance of CPS remains largely uncertain, it is important to recognize that severe cardiopulmonary complications do occur. Therefore, patients should undergo cardiac and/or pulmonary evaluations, and symptoms should not be simply dismissed as benign and solely related to cannabis use.[16]

The pathophysiology by which cannabis affects so many aspects of the cardiopulmonary system is poorly understood, but given that cannabis contains over 400 different compounds, including 100 different cannabinoids, the pathology is likely to involve various specific pathways.[12] While a thorough discussion of these pathways is beyond the scope of this article, several excellent reviews discuss these pathways and possible mechanisms of action of cannabinoids.[9,13,18] Cannabinoid protein receptors can be found throughout the cardiovascular and pulmonary tissues. This includes vascular smooth muscle cells and endothelium, the myocardium, as well as respiratory dendritic and bronchi cells, circulating blood cells, and the autonomic nervous system.[3,11,12] The cardiopulmonary toxicity of cannabis is also affected by age, comorbidities, dose, type of cannabinoids used, duration of use, and concomitant use of other illicit drugs.[10–12] In addition, given the expanding use of cannabis edibles and the likelihood that they contain substantial levels of D9-tetrahydrocannabinol (THC), clinicians should inquire about food or beverage products that have been infused with cannabis extract.[2]

Synthetic cannabinoids and cannabimimetics are also gaining in popularity. High potency and easy access have likely contributed to their use. In addition, many conventional drug screening tests are unable to identify them.[8] These illegal substances include hundreds of synthetic compounds made by various chemical alterations of THC to increase its affinity for cannabinoid receptors and prolong the duration of action. Many synthetic compounds also have active metabolites that add significantly to the risk of CPSs and disease.[8] Overall, the effects of synthetic cannabinoids and their metabolites can be severe, unpredictable, or even life-threatening. Finally, as the number of states that legalize cannabis increases, an inconsistent patchwork of safety regulations has expanded. As cannabis remains federally illegal, there are no uniform standards. Legally sold marijuana may be contaminated with pesticides, heavy metals, foreign matter, yeast and mold, solvents, and banned pathogens, including Aspergillus, Salmonella, and E. coli.[19]

This study has several important limitations. Given that this was a retrospective review of medical records, there is always variability in clinical assessment and documentation by different clinicians. Thus, documentation of outcome variables may not have been consistent. This could have been mitigated by a prospective observational study and by setting strict guidelines to gather data in a more uniform manner. However, an observational trial

Table 3. Areas for future cannabis research.

- Conducting longitudinal studies to assess the long-term effects of cannabis use on physical health, cognitive function, and overall well-being, especially in heavy or chronic users.
- Medical applications of cannabis and its cannabinoids for various conditions, including pain management, epilepsy, anxiety, and other health issues. Research should focus on identifying safe and effective dosages and delivery methods.
- Studying the complex relationship between cannabis use and mental health outcomes, including the potential risks of cannabis use for individuals with or at risk of psychiatric disorders.
- Analyzing patterns of cannabis use, including frequency, dosage, and method of consumption, to better understand their impact on health outcomes.
- Investigating the effects of early and adolescent cannabis use on brain development, mental health, and long-term outcomes, given that the brain is still developing during these years.
- Exploring the potential benefits and risks of cannabis use among older adults, including its impact on pain management, sleep, and age-related conditions.
- Advancing our understanding of the pharmacological properties of various cannabis strains, cannabinoids, and terpenes to optimize therapeutic outcomes and minimize side effects.
- Evaluating the social, economic, and public health impacts of cannabis legalization and regulation in different jurisdictions, including effects on substance abuse rates, crime, and public health outcomes.
- Developing interventions and treatments for individuals with cannabis use disorder and studying the effectiveness of harm reduction strategies.
- Researching the diversity of cannabis strains and traditional uses in different regions worldwide to better understand cultural practices and potential therapeutic applications.

will take longer to complete and will be more costly. Our sample population was drawn from 13 counties located in Michigan. Although we utilized a mix of urban and rural settings for our study population, it is not known how patient demographics and characteristics in other settings might differ from our patients. For example, over one-third of our population had comorbidities. It is not clear if the presenting symptoms or outcomes are solely due to cannabis or from exacerbation of chronic illness (e.g., bronchitis, ischemic heart disease). Almost 18% of our population also had a history of polysubstance abuse, which might predispose them to cardiopulmonary toxicity. Testing for these substances in the ED is rarely helpful for treatment due to the time required to get toxicology results.[17]

Despite an increased need for research following the legalization of cannabis, our understanding of its genetic and chemical diversity, public health risks, and medical benefits is still critically incomplete.[20] Table 3 lists some areas of research that warrant further investigation. Future research in cannabis-related cardiopulmonary complications should aim to provide a comprehensive understanding of the risks, mechanisms, prevention, and treatment strategies associated with cannabis use in relation to heart and lung health. This knowledge can inform public health guidelines, medical practice, and policy decisions regarding cannabis use.

CONCLUSIONS

This is the first epidemiologic study in the U.S. to specifically examine the prevalence, clinical features, and disposition of cannabis cardiopulmonary toxicity in the ED. By being community-based, this study offers insights into the real-world experiences and outcomes of individuals who seek emergency care due to cannabis toxicity. This knowledge is vital for healthcare practitioners, public health officials, and policymakers to make informed decisions about cannabis regulation, education, and healthcare provision.

Conflict of interest and funding

The authors declare that they have no conflict of interest, and no funding was provided for this research study.

Previous Presentation

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REFERENCES

1. O'Keefe EL, Dhore-Patil A, Lavie CJ. Early-onset cardiovascular disease from cocaine, amphetamines, alcohol,

and marijuana. Can J Cardiol 2022; 38(9): 1342–51. doi: 10.1016/j.cjca.2022.06.027
2. Lewis B, Fleeger T, Judge B, Riley B, Jones JS. Acute toxicity associated with cannabis edibles following decriminalization of marijuana in Michigan. Am J Emerg Med 2021; 46: 732–5. doi: 10.1016/j.ajem.2020.09.077
3. Finn K. Cannabis in medicine. New York: Springer International Publishing; 2020.
4. Montoya ID, Weiss SRB. Cannabis use disorders. New York: Springer; 2019.
5. Hall W, Solowij N. Adverse effects of cannabis. Lancet 1998; 352: 1611–6. doi: 10.1016/S0140-6736(98)05021-1
6. Schmid Y, Scholz I, Mueller L, Exadaktylos AK, Ceschi A, Liechti ME, et al. Emergency department presentations related to acute toxicity following recreational use of cannabis products in Switzerland. Drug Alcohol Depend 2020; 206: 107726. doi: 10.1016/j.drugalcdep.2019.107726
7. Schmid Y, Galicia M, Vogt SB, Liechti ME, Burillo-Putze G, Dargan PI, et al. Differences in clinical features associated with cannabis intoxication in presentations to European emergency departments according to patient age and sex. Clin Toxicol (Phila). 2022; 60(8): 912–9. doi: 10.1080/15563650.2022.2060116
8. Singh A, Saluja S, Kumar A, Agrawal S, Thind M, Nanda S, et al. Cardiovascular complications of marijuana and related substances: a review. Cardiol Ther 2018; 7(1): 45–59. doi: 10.1007/s40119-017-0102-x
9. 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; 9(6): 1925. doi: 10.3390/jcm9061925
10. Pacher P, Steffens S, Haskó G, Schindler TH, Kunos G. Cardiovascular effects of marijuana and synthetic cannabinoids: the good, the bad, and the ugly. Nat Rev Cardiol 2018; 15(3): 151–66. doi: 10.1038/nrcardio.2017.130
11. Richards JR. Mechanisms for the risk of acute coronary syndrome and arrhythmia associated with phytogenic and synthetic cannabinoid use. J Cardiovasc Pharmacol Ther 2020; 25(6): 508–22. doi: 10.1177/1074248420935743
12. Weresa J, Pędzińska-Betiuk A, Mińczuk K, Malinowska B, Schlicker E. Why do marijuana and synthetic cannabimimetics induce acute myocardial infarction in healthy young people? Cells 2022; 11(7): 1142. doi: 10.3390/cells11071142
13. Subramaniam VN, Menezes AR, DeSchutter A, Lavie CJ. The cardiovascular effects of marijuana: are the potential adverse effects worth the high? Mo Med 2019; 116(2): 146–53.
14. Van Keer JM. Cannabis-induced third-degree AV block. Case Rep Emerg Med 2019; 2019: 5037356. doi: 10.1155/2019/5037356
15. McHugh ML. Interrater reliability: the kappa statistic. Biochem Med (Zagreb). 2012; 22(3): 276–82. doi: 10.11613/BM.2012.031
16. Gresnigt F, van den Brink LC, Hunault C, Franssen E, de Lange D, Riezebos R. Incidence of cardiovascular symptoms and adverse events following self-reported acute cannabis intoxication at the emergency department: a retrospective study. Emerg Med J 2023; 40(5): 357–8. doi: 10.1136/emermed-2022-212784
17. Britch SC, Walsh SL, Vickers-Smith R, Babalonis S, Slavova S. Cannabinoid poisoning-related emergency department visits and inpatient hospitalizations in Kentucky, 2017 to 2019. Subst Use Misuse 2023; 58(1): 66–76. doi: 10.1080/10826084.2022.2148478
18. Renard J. Clearing the smoke on cannabis: respiratory and cardiovascular effects of cannabis smoking. Ottawa: Canadian Centre on Substance Use and Addiction; 2020. Available from: https://www.ccsa.ca/clearing-smoke-cannabis-respiratory-and-cardiovascular-effects-cannabis-smoking-report [cited 18 September 2023].
19. Jameson LE, Conrow KD, Pinkhasova DV, Boulanger HL, Ha H, Jourabchian N, et al. Comparison of state-level regulations for cannabis contaminants and implications for public health. Environ Health Perspect 2022; 130(9): 97001. doi: 10.1289/EHP11206
20. Piomelli D, Solomon R, Abrams D, Balla A, Grant I, Marcotte T, et al. Regulatory barriers to research on cannabis and cannabinoids: a proposed path forward. Cannabis Cannabinoid Res 2019; 4(1): 21–32. doi: 10.1089/can.2019.0010