

What is the Association of Cannabis Consumption and Cardiovascular Complications?

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Introduction

Cannabis is a frequently used recreational drug that potentially imposes several health consequences. While the medicinal use of cannabis is legal in several countries, its possession in small quantities for the purpose of personal use has a worldwide trend to become decriminalized and effectively legal.¹ In the author's knowledge, the accessibility and overall usage of cannabis is steadily increasing. In fact, it has been advocated that marijuana is the most popularly used illegal drug worldwide.² The current wave of decriminalization is expected to produce a more widespread recreational use, and it is imperative that cardiologists are aware of the potential cannabis-associated cardiovascular complications. This article is an editorial presenting several reported cases in the literature implicating marijuana smoking in cardiovascular complications, and we concisely discuss the potential underlying mechanisms as well as the clinical implications of this emerging phenomenon.

What is the Incidence of Cannabis-Induced Cardiovascular Complications?

In France, serious cases of abuse and dependence in response to the use of psychoactive substances are officially reported to the nationally controlled French Addictovigilance Network.

From 2006 to 2010, 1.8% of all cannabis-related reports (35/1979) were cardiovascular complications.³ According to this network, cardiovascular complications were a lot more prominent in men (85.7%) and people having an average age of 34.3 years. It is also important to note the extreme seriousness of reported events, with a death rate of 25.6%.

Cannabis-Induced Acute Coronary Syndromes

The use of cannabis is not usually regarded as an established risk factor for acute coronary syndromes. However, it has been illustrated in scientific literature that several cases of acute coronary syndrome were attributed to the use of cannabis. A case report documented an exercise-induced myocardial infarction with complete occlusion of the proximal right coronary artery in an otherwise healthy 24-year-old individual without any risk factors for coronary artery disease.⁴ This episode was noted, with the implementation of intravascular ultrasound (IVUS), to have occurred in the setting of a disrupted atherosclerotic plaque. In another case report, a 21-year-old regular user of cannabis suffered an anterior myocardial infarction after participation in sports.⁵ Despite the fact that a large amount of thrombus was retrieved from the left anterior descending artery, IVUS identified no evidence of underlying atherosclerosis in the site of



occlusion. The discrepancy of the underlying histopathologic substrate in these two cases illustrates the complexity in understanding the underlying causative linkage and pathogenic mechanism. Despite the uncertainty regarding its pathophysiology, acute coronary syndromes have a pronounced trend of occurring in the first hour after inhalation of marijuana.⁶ Cannabis is also established to aggravate coronary ischemia in patients with known long-standing coronary artery disease and potentially trigger a myocardial infarction.⁷

Connection of Cannabis Use with Sudden Cardiac Death

A case series reports three young patients, where the recent use of marijuana is suggested to have caused cardiac arrest.⁸ The first patient was found collapsed at home in asystole and required cardiopulmonary resuscitation (CPR) for restoration of spontaneous circulation (ROSC). The coronary angiography identified a pronounced and diffuse arterial vasospasm, and no intervention was required. The other two patients were found in ventricular fibrillation and required electrical cardioversion for ROSC. Malignant arrhythmia was triggered by myocardial ischemia in the setting of occlusion of a coronary artery. Further information that associate the use of cannabis with malignant arrhythmologic events are drawn from a case report, where multiple pauses, the longest lasting up to 5.8 seconds, were identified using a 24-hour Holter monitor in a 21-year-old student with frequent inhalation of marijuana.⁹ The linkage with arrhythmologic risk is also implied in a report of intermittent presentation of type 1 Brugada electrocardiographic pattern in a 42-year-old man with repeated use of cannabis.¹⁰ Total abstinence of the substance confirmed resolution of the electrocardiographic abnormality, and no further investigation was required. Ventricular tachycardia is also reported to have occurred as a result of marijuana use in a heart transplant patient.¹¹ Literature exploration isolated two more cases of unexpected death possibly because of suspected fatal cannabis intoxication.¹² In these cases, full postmortem investigations, including autopsy, toxicological, histological, immunohistochemical, and genetical examinations, identified no specific cause. The exclusion of other causes of death reasonably leads to the assumption of fatal cardiovascular complications evoked by smoking cannabis.

Paroxysmal Atrial Fibrillation Following Marijuana Intoxication

Marijuana smoking has been shown to exert adverse effects on the cardiovascular system and often causes well-tolerated tachycardia and hypotension. It is also reported to be a possible cause of paroxysmal atrial fibrillation.¹³ The inhalation of marijuana is suggested to be a precursor of atrial tachycardia in a similar way to the effect of acute alcohol consumption.¹⁴

Cannabis-Associated Cerebrovascular and Peripheral Arterial Disease

Cannabis use is found to be associated with stroke and lower limb arteritis. Unusual sites of cerebral infarcts in young patients should point toward the potential use of illicit drugs.¹⁵ Most acute cerebrovascular episodes have been reported to occur within one hour of smoking marijuana.¹⁶ A predilection was noted in the occurrence of strokes in the posterior cerebral circulation. According to the same literature review, the involvement of peripheral arterial system was mostly unilateral and occurred more frequently in young men. In general, the outcome of reported arterial manifestations among cannabis smokers is correlated with persistent withdrawal. The importance of total cannabis abstinence in affected individuals is also shown in a different case series, where 5 out of 17 patients with cannabis-related stroke suffered a recurrent event after re-exposure to cannabis.¹⁷ Cannabis arteritis has not yet been able to be confirmed as a specific diagnostic entity, but there is a definite linkage. A formal association between cannabis usage and the occurrence of thromboangiitis obliterans is very difficult to be demonstrated, since consumption of smoking is very common (97%) in such individuals.¹⁸

Takotsubo Cardiomyopathy in a Marijuana User

A case of Takotsubo cardiomyopathy was described in a 32-year-old female who recently ingested marijuana after a period of abstinence.¹⁹ The author suggests as a possible explanation to this phenomenon the endocannabinoid receptors, which are expressed in the myocardium.

Myopericarditis as a Complication of Marijuana Use

A relatively unusual complication of marijuana use is recurrent myopericarditis.²⁰ In this particular case report, a 29-year-old man presented with consecutive episodes of chest pain aggravated by cough and deep inspiration and relieved by sitting and leaning forward. Typical electrocardiographic evidence along with elevation of myocardial enzymes confirmed the suggested diagnosis. Treatment with ibuprofen resulted in resolution of symptoms and electrocardiographic abnormalities, but re-exposure to marijuana resulted in recurrence of clinical condition.

Pathogenesis of Cannabis-Induced Cardiovascular Complications

The active substance of cannabis is 9-9-tetrahydrocannabinol (9-9-THC). Several pharmacological studies were conducted on animals in order to investigate the possible effect of this substance on the cardiovascular system.²¹ Most of its action is suggested to occur through specific receptors in the cardiovascular regulatory center and the peripheral autonomic system. The effect of cannabis is dose dependent. At a high dose, an increased heart rate is observed, presumably because of peripheral inhibition of cardiac parasympathetic fibers.²² Heart rate acceleration is suggested to be implicated in the pathogenesis

of acute coronary episodes. The potential arrhythmogenic effect of cannabis is suggested to be caused by the direct effect on autonomic activity or on Purkinje fibers.²³ Cannabis is also advocated to have a direct effect on coronary microcirculation. The combination of alcohol with marijuana could potentially increase the cardiac toxicity of 9–9-THC by alteration of atrial refractoriness and conduction velocity. As both drugs are frequently taken together, this observation may be of great clinical importance in the evaluation of young patients with arrhythmologic events. In order to document the linkage of cannabis use with sudden arrhythmologic cardiac death, it is important to measure plasma in the toxicology screen in coroners' cases where urine cannabinoids are positive.²⁴ A positive urine cannabinoid immunoassay alone is insufficient evidence in the linkage of acute cardiac death and cannabis.

Conclusion

The evidence reported in this article point toward an undisputed linkage between cannabis consumption and potentially lethal cardiovascular complications. It is very important to emphasize that a clearly defined causal role of this linkage is not able to be clearly demonstrated because of confounding variables. The exact amount of ingested cannabis in the cases presented was not able to be determined, since it is processed in a non-authorized setting. The changing legal landscape and the scientific evidence illustrated above strongly highlight the necessity of intensified research regarding the safety of cannabis use. Physicians need to become aware of this spectrum of clinical presentations, not only for timely diagnosis and treatment but also mostly for effective counseling and prevention.

Author Contributions

Conceived the concepts: IP. Wrote the first draft of the manuscript: IP. Made critical revisions: IP. The author reviewed and approved of the final manuscript.

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