A Modern Respiratory Therapist Guide to the Health Complications of Cannabis Use

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Abstract

Although cannabis law reform has swept our nation, respiratory therapists have been left in the dark about the health complications associated with its use. Most respiratory therapists have received little to no formal education on these complications. The intent of this literature review is to educate respiratory therapists on the unique physiologic manifestations of cannabis-related health complications. By gaining knowledge on this topic, respiratory therapists will be better prepared to diagnose and develop treatment strategies for patients presenting with issues related to cannabis use.

KEYWORDS:
Takotsubo cardiomyopathy, cannabis health complications, cannabis disorders, respiratory

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Purpose

Reforms allowing for the personal (recreational) use of cannabis have swept our nation. This process began more than a decade ago, with the states of Colorado and Washington first legalizing recreational cannabis use in November of 2012 (Dills et al., 2021). As of November 2020, thirteen states have followed suit by allowing cannabis to be used by adults over the age of twenty-one: Alaska, Oregon, California, Nevada, Maine, Vermont, Massachusetts, Michigan, Illinois, New Jersey, South Dakota, Arizona, and Montana (Dills et al., 2021). Ultimately, the legalization of cannabis has catalyzed an increase in the number of cannabis users over the last decade, with exponential growth seen within the last five years and reaching levels not seen since the 1980s (Ann Arbor: Institute for Social Research, 2021).

There are numerous motives behind modern cannabis law reforms. One of the most commonly referenced is the relative safety of cannabis compared to other controlled substances (Lachenmeier & Rehm, 2015). However, the potential health risks due to its use have eluded not only the population at large, but the vast majority of the healthcare community, as well (Ghonaim, 2018). Unfortunately, the topic of cannabis and the endocannabinoid system have yet to be included in most modern healthcare education programs (Mann, 2021).

The lack of common understanding surrounding an accurate health risk assessment of cannabis use is inherently linked to the complex and varying chemical compounds found within modern cannabis (Atakan, 2012). In total, over 400 chemicals have been identified within cannabis and approximately 60 of these chemicals, known as cannabinoids, are exclusively unique to this substance (Dewey, 1986). Some cannabinoids such as delta-9-tetrahydrocannabinol (Δ-9-THC) and cannabidiol (CBD), have been shown to have opposing effects, further complicating our understanding of the chemical interactions within the body from cannabis use (Pamplona & Takahashi, 2011). It is also known that individual users can respond to the varying chemical mixtures within cannabis in drastically different ways, based on variations within their own endocannabinoid systems (Atakan, 2012).

Within this review, it was found that many of the known health risks of cannabis use are associated with the most frequent forms of consumption: Smoking and vaping (Boyd et al., 2021; Tashkin, 2013). The inherent pulmonary and cardiovascular complications from these consumption methods are well within the scope of practice of registered respiratory therapists.

Introduction

Patients may initially deny using cannabis because of the associated social stigmas, professional implications, legal ramifications, and false perceptions about the substance being completely harmless (Compton et al., 2016; Marcoux et al., 2013). Some of the signs, symptoms, and health complications cannabis users present with are specific or unique to this substance. An example is those patients with cannabis hyperemesis syndrome, from which patients present with cyclic vomiting and nausea that is only relieved by hot showers (Blumentrath et al., 2017). This, in turn, makes identifying the causation (cannabis use) of their presenting conditions relatively straightforward, regardless of the patient openly admitting to using cannabis or not.

However, some of the other signs, symptoms and conditions associated with cannabis use, such as chronic bronchitis or frequent pneumonia infections, are not unique to cannabis. This can make identifying the cannabis-based causation more difficult to identify, especially when the patient has not admitted to cannabis use. Some of the more generic signs and symptoms could be incorrectly assumed as the result of numerous other common diseases and illnesses. This can potentially lead to an inaccurate diagnosis, a slowed treatment process and readmissions due to continued cannabis use. Ultimately, a healthcare team lacking a formal education in identifying health conditions due to cannabis use can waste precious critical care resources on diagnostic testing, ineffective interventions, treatments, and therapies.

Some of the most serious health complications from cannabis use can include life-threatening cardiopulmonary conditions such as myocardial infarctions and cerebral vascular accidents. The need for critical care staff—specifically respiratory therapists—to be able to identify the signs, symptoms and causes of cannabis-related health conditions is integral to effective healthcare in the modern environment. Furthermore, the ability to identify patients who are at a high risk for complications from cannabis consumption is paramount in the preventative education process surrounding cannabis use.

Research Question

The aim of this literature review was to compile a list of the currently known health complications associated specifically with cannabis use (short-term or one-time use) and abuse (long-term, frequent use) from modern, peer-reviewed medical journals. Emphasis was placed on identifying individuals who may have elevated risk factors for complications due to cannabis use, the unique clinical presentations associated with cannabis-induced health conditions, and the pathophysiology of health conditions associated with cannabis use.
Methods

For a health condition associated with cannabis consumption to be included in this review, it must (1) be documented in a peer-reviewed medical journal, (2) have a direct or temporal relationship to cannabis, and (3) cause a severe health complication, for which a patient may be admitted for critical care.

The search strategy to identify studies for this review was initially based on compiling a list of resources cited in presentations by the two most renowned medical doctors who specialize in the pathophysiology of cannabis-related health conditions: Donald P. Tashkin and Paul Oh (Oh, 2018; Tashkin, 2017). After creating a list of the research studies cited in their presentations, the original source articles were located via online search databases including, but not limited to, The United States National Library of Medicine (https://pubmed.ncbi.nlm.nih.gov), Google Scholar (https://scholar.google.com), and Northern Kentucky University’s W. Frank Steely Library (https://inside.nku.edu/library.html). These databases were also searched for additional research articles based on health conditions related to cannabis use. Search terms included cannabinoid hyperemesis syndrome, stress cardiomyopathy, takotsubo, cannabis and marijuana. All found articles were read in full, then screened and separated based on the above inclusion criteria. Articles that met the criteria were designated to be included in this literature review.

Results

Fourteen articles met the qualifications for inclusion in this review. Surprisingly, in each of the qualified articles, health conditions associated either directly or indirectly with cardiopulmonary function were identified.

Stress cardiomyopathy was the most frequently cited condition. Eight of the included articles focused on stress cardiomyopathy and its temporal relationship to cannabis use (Alliu et al., 2017; Del Buono et al., 2017; Greene, 2021; Kaushik et al., 2011; Meera et al., 2020; Nogi et al., 2014; Sanchez et al., 2019; Singh et al., 2017). Five of the articles referenced alternative titles for this condition, including takotsubo cardiomyopathy (Nogi et al., 2014; Sanchez et al., 2019), transient apical ballooning syndrome (Alliu et al., 2017) and broken-heart syndrome (Del Buono et al., 2017; Greene, 2021).

Myocardial infarction was identified as a health risk of cannabis use in three articles (Chami & Kim, 2019; Del Buono et al., 2017; Mittleman et al., 2001).

Changes to pulmonary tissues and/or deficits to immune function of the pulmonary system were the central focus of three articles (Tashkin, 2013; Tashkin, 2018; Tashkin & Roth, 2019). All of these articles were authored by Donald Tashkin, the renowned pulmonologist and professor specializing in this field of study, and whose presentation was used as a launch pad for identifying research studies to be included in this literature review. Frequent respiratory infections were also listed as a major health concern for cannabis users in two of the articles included in this review (Kagen et al., 1983; Ungerleider et al., 1982).

Lastly, a temporal relationship between cerebral vascular accidents and cannabis use was identified in two articles (Meera et al., 2020; Uhegwu et al., 2015).

Discussion

Stress Cardiomyopathy

Stress cardiomyopathy is a relatively rare form of non-ischemic cardiomyopathy that typically presents with symptoms similar to that of an acute myocardial infarction (Alliu et al., 2017). Other common names for this condition include takotsubo cardiomyopathy, transient apical ballooning syndrome, and broken-heart syndrome. These names are all based on the observed balloon shape of the left ventricle (e.g., takotsubo being an oblong shaped octopus’ trap) or the related stress factors thought to be responsible for this condition (e.g., a broken heart from the stress of a lost loved one). Stress cardiomyopathy has traditionally been observed in middle-aged mothers (females) dealing with very difficult life circumstances, such as those seen in war or extreme poverty. In males, this condition is extremely rare. However, it has been found that males who use cannabis have a fivefold increased risk for stress cardiomyopathy and similar cardiac events (Sanchez et al., 2019).

Symptoms of stress cardiomyopathy frequently lead to the suspicion of a myocardial infarction (heart attack). Most myocardial infarctions are the result of a major blockage in one of the coronary arteries; yet in stress cardiomyopathy, the coronary arteries are not blocked (Meera et al., 2020). Although it has yet to be proven, excessive catecholamine release has been theorized as the main pathogenesis of stress cardiomyopathy (Alliu et al., 2017). A widely accepted theory is that cannabis use directly creates an abrupt increase in catecholamines. This increase has been observed to cause tachycardia and the elevation of both systolic and diastolic blood pressure, which could lead to cardiac conditions such as stress cardiomyopathy (Sanchez et al., 2019). However, there is a second and equally accepted theory for the increased incidence of cardiac events (such as stress cardiomyopathy) in cannabis users that points...
to the endocannabinoid system and its interaction with the autonomic nervous system's regulation of cardiac function (Singh et al., 2017).

Research from Green (2021) showed a twofold increase in the odds of developing stress cardiomyopathy in nondependent (below addiction-level use) cannabis users with a 95% confidence interval. Surprisingly, this association had no significance in dependent (addiction-level) cannabis users (Greene, 2021). Another case of stress cardiomyopathy connected to cannabis use was documented in the state of Hawaii. A 32-year-old female medical marijuana patient presented with a relatively well-known cannabis-related condition called cannabis hyperemesis syndrome, which is characterized by nausea and vomiting that is only relieved by taking a hot shower (Nogi et al., 2014). However, her EKG showed “dynamic T-wave changes,” which are not associated with cannabis hyperemesis syndrome (Nogi et al., 2014). Her echocardiogram was interpreted as “ventricular wall abnormalities suggestive of stress cardiomyopathy” (Nogi et al., 2014). The patient admitted to recently “ingesting” cannabis after abstaining from use for a period of around three months (Nogi et al., 2014).

Research from Sanchez et al. (2019) highlighted the case of a 50-year-old male with a history of hypertension and “regular” cannabis use. He presented with chest pain radiating to his back. Due to an abnormal electrocardiogram and positive cardiac biomarkers for acute coronary syndrome, a coronary angiography was conducted. Surprisingly, no significant coronary obstruction was found. However, a left ventriculogram showed the “characteristic apical ballooning” of stress cardiomyopathy (Sanchez et al., 2019).

Meera et al. (2020) reported on the case of a 56-year-old male with no known past cardiac history who presented with symptoms of confusion, aphasia, and left-sided weakness. His wife reported increased somnolence, poor appetite, and lethargy for a few days. His blood pressure was 148/105 mmHg with a heart rate of 102 beats per minute (Meera et al., 2020). Computed tomography (CT) and magnetic resonance imaging (MRI) revealed “no acute intracranial pathology” (Meera et al., 2020). His chest X-ray revealed “pulmonary congestion” and a 12-lead electrocardiogram showed an ST segment depression and QTc interval prolongation (Meera et al., 2020). An echocardiogram revealed a mildly dilated left ventricle cavity with severe hypokinesis resulting in a “markedly reduced ejection fraction” (Meera et al., 2020). However, a coronary angiography showed no signs of obstruction. When questioned, the patient denied any recent emotional stress, but admitted to using cannabis heavily for several days before this presentation.

Kaushik et al. (2011) researched a case of recurrent stress cardiomyopathy in a 59-year-old woman presenting with angina. She denied any recent physical or emotional stressors, but admitted to years of dependent cannabis use. Physical examination revealed jugular venous pulsation, bilateral lung crackles, and left ventricular gallop (Kaushik et al., 2011). A 12-lead electrocardiogram showed poor R-wave progression, ST-segment elevation, and T-wave inversion (Kaushik et al., 2011). An echocardiogram was used to estimate the left ventricular ejection fraction, which was found to be 20% to 25%; this is below the normal range of 50%-75% (Kaushik et al., 2011). The echocardiogram was also used to identify severe hypokinesis of the apical and midsegments (Kaushik et al., 2011). Cardiac catheterization revealed normal epicardial coronaries, and a ventriculogram was consistent with apical ballooning indicative of stress cardiomyopathy (Kaushik et al., 2011). This patient had four admissions in the previous three years, with similar clinical course and diagnostic findings (Kaushik et al., 2011). She had admitted cannabis use and tested positive for Δ-9-THC on each of the previous occurrences. Therefore, her final diagnosis was recurrent stress cardiomyopathy due to cannabis abuse (Kaushik et al., 2011).

**Myocardial Infarction**

One documented case of stress cardiomyopathy with a temporal relation to cannabis use resulted in the death of an otherwise healthy 23-year-old woman. The cause of death was documented as cardiac arrest (myocardial infarction) due to ventricular fibrillations associated with apical ballooning syndrome (del Buono et al., 2017). It was found that she had smoked cannabis a few times over the days leading up to her death. Her autopsy revealed subendocardial hemorrhaging, which hints at the pathophysiology of this poorly-understood condition (del Buono et al., 2017). Subendocardial hemorrhaging (as observed in this patient with apical ballooning syndrome) has been found to occur the most frequently in the upper part of the interventricular septum, where the left branches of the atrioventricular bundle are located, suggesting a possible mechanism for the ventricular arrhythmia (Seidl, 2005).

A study conducted by Chami and Kim (2019) looked at 292,770 patients with a history of cannabis abuse and compared their risk for myocardial infarction (MI) to 10,542,348 patient controls matched for age and sex. This study found the three-year cumulative incidence of MI was significantly higher in the cannabis abuse group than in controls, concluding a 1.37% vs. 0.54% relative risk factor with a 95% confidence interval. Women aged 40-44 years and men aged 35-39 years were the highest-risk groups, reaching up to 4.78% relative risk (Chami & Kim, 2019). Furthermore, the subgroup of dependent cannabis users showed a significant correlation to myocardial incidents (adjusted odds ratio: 1.72; 95% CI). This was independent of advanced age, sex, hypertension, coronary artery disease, diabetes, and other substance abuse (Chami & Kim, 2019). A research study from Mittleman et al. (2001) was based on
interviewing 3,882 patients with previous acute myocardial infarctions. Of the 3,882 patients included in their study, 124 (3.2%) reported smoking cannabis within the last year. Thirty-seven patients admitted to smoking cannabis within 24 hours prior to the onset of their symptoms, and nine of the 3,882 patients smoked cannabis within one hour prior to symptom onset. Mittleman et al. (2001) concluded that the risk of myocardial infarction onset was elevated 4.8 times over baseline (95% CI) in the 60 minutes following cannabis use, and that the elevated risk rapidly decreased thereafter.

**Similarities between Cannabis and Tobacco Pulmonary Pathophysiology**

In 2013, Tashkin conducted research that found an association between smoking cannabis and visible and microscopic injury to the large airways. Interestingly, the injuries were found to subside after cessation (Tashkin, 2013). Tashkin looked further into this concept when he conducted his 2018 research study that was designed to compare the bronchial mucosa of a non-smoker, a cannabis smoker, and a tobacco smoker via bronchoscopies with bronchial biopsy. The cannabis smoker’s large airways showed less reddening of tissues (erythema) compared to the tobacco smoker (Tashkin, 2018). Conversely, the small airways (bronchioles) of the cannabis smoker showed substantially more swelling (edema) compared to the tobacco smoker (Tashkin, 2018). A third study conducted by Tashkin and Roth in 2019 found that tobacco smokers and frequent cannabis smokers both show similar magnitudes of destruction to ciliated epithelium cells, hyperplasia of mucus-secreting goblet cells and cellular disorganization. Therefore, it is postulated that the frequency of chronic cough and the overproduction of sputum between cannabis smokers and tobacco smokers is similar (Tashkin & Roth, 2019).

One major difference between tobacco smoke and cannabis smoke is their effect on alveolar macrophages. Tashkin and Roth (2019) found that the alveolar macrophages in cannabis smokers show a reduced ability to produce cytokine as well as a deficit in antimicrobial and fungicidal activity. This downregulation of alveolar macrophage activity has never been observed in the cells of tobacco smokers (Tashkin & Roth, 2019). They speculated that the known immunosuppressive effect of Δ-9-THC, along with the presence of CBR2 (cannabinoid receptors) on alveolar macrophage cells, are both responsible for the downregulation of activity (Tashkin & Roth, 2019).

Another potential pathophysiologic difference in cannabis smokers was noted in Tashkin’s 2013 study, which referenced several case reports that implicated frequent smoking of cannabis as a possible etiologic factor in pneumothorax, pneumomediastinum and bullous lung disease. However, it was noted that an epidemiologic study has not been conducted to produce evidence of the “causal link” between these conditions and smoking cannabis (Tashkin, 2013).

**Frequent Respiratory Infections**

Even though the evidence is generally inconclusive regarding the relative risk factor for lower respiratory tract infections, it has been postulated that smoking cannabis predisposes users to these infections in a few different ways (Tashkin, 2018). As previously stated, damage to ciliated epithelial cells, cellular disorganization and the hyperplasia of mucus-secreting goblet cells have been observed in both tobacco smokers and cannabis smokers alike (Tashkin, 2018). These cellular changes lead to an increase in mucus production, while simultaneously impairing the mucociliary escalator. Ultimately, this creates an ideal substrate for pathogenic microbial organisms like *Pseudomonas aeruginosa* to colonize in the lower respiratory tract (Tashkin, 2018). However, as previously mentioned, in cannabis smokers the downregulation of alveolar macrophage activity clearly perpetuates the frequency and severity of these infections in the respiratory tract. In addition to an increased likelihood of infections such as *P. aeruginosa*, the cumulative cellular changes observed in frequent cannabis smokers also provides a clue into the longstanding association between cannabis use and chronic bronchitis symptoms (Tashkin & Roth, 2019).

An additional mechanism for an increased risk of pneumonia in cannabis smokers was identified in a case study from Kumar et al. (2018). The study was based on a 23-year-old male who presented with a three-day history of fever, hemoptysis, and dyspnea (Kumar et al., 2018). Palpation and auscultation of the chest revealed crepitations with decreased breath sounds on the left (Kumar et al., 2018). CT imaging helped identify an area of necrotizing pneumonia involving the left upper lobe (Kumar et al., 2018). Upon questioning, the patient admitted to using a “small water pipe or bong” to smoke cannabis daily over the span of four years. Interestingly, the patient elaborated that the bong was being used for its supposed benefit of filtering the cannabis smoke. Cultures were obtained not only from the patient’s sputum and pleural fluid, but also from the water in the bong. All three cultures grew *P. aeruginosa* (Kumar et al., 2018). It is theorized that during the process of inhaling cannabis smoke through the bong, the patient was inadvertently and repeatedly inhaling water aerosols contaminated with *Pseudomonas aeruginosa*, which had led to the necrotizing pneumonia infection.

A final factor adding to the increased likelihood of respiratory infections in cannabis smokers is the frequency at which cannabis has been found to be contaminated with *Aspergillus fumigatus* and potentially pathogenic gram-negative bacteria (Kagen et al., 1983; Tashkin, 2018; Ungerleider et al., 1982). The effects of combusting *A. fumigatus* and bacteria during the
smoking process are unknown; however, the potential consequences of their introduction into lung tissues of cannabis smokers—whose lungs are already immunocompromised—provides another possible mechanism for an increased risk of respiratory infections (Tashkin, 2018).

**Cerebral Vascular Accidents**

Accounts of cerebral vascular accidents (strokes) from cannabis use have been reported (Uhegwu et al., 2015). The postulated etiologies include reversible cerebral vasospasms, vasculitis, postural hypotension, and increased carboxyhemoglobin leading to reduced oxygen transportation capacity (Uhegwu et al., 2015). Reversible cerebral vasoconstriction syndrome (RCVS) is a unifying term for a variety of cerebral vasospasm activity which results in the clinical manifestation of cerebral ischemia (Uhegwu et al., 2015). RCVS, sometimes referred to as drug-induced cerebral angiopathy, is typically characterized by a transient, multifocal, cerebral arterial vasoconstriction and dilatation cycle. Research from Uhegwu et al. (2015) found that cannabis abuse is a common etiologic factor for RCVS, as well as other types of cerebral vascular accidents.

The previously mentioned case study on stress cardiomyopathy from Meera et al. (2020) also included elements of a reversible cerebral vascular accident. The 56-year-old male patient who admitted to using cannabis heavily for several days before this presentation had no known cardiac or neurological history. He presented with symptoms of confusion, aphasia, and left-sided weakness. His wife also has noticed left-sided facial droop and impaired coordination over the previous few days. Physical examination revealed that his motor strength was reduced in the left upper and lower extremities (Meera et al., 2020). However, due to the reversible nature of RCVS, CT and MRI revealed “no acute intracranial pathology” (Meera et al., 2020). The patient was drug screened and only tested positive for Δ-9-THC with zero traces of cocaine, opioids, amphetamines, barbiturates, benzodiazepines, or alcohol (Meera et al., 2020). Blood glucose and thyroid function tests were also within normal range (Meera et al., 2020). After being monitored for a few days, the patient was discharged, yet continued to experience transient neurological deficit, with the only known contributing factor being heavy cannabis use.

**Conclusion**

According to the United Nations 2020 World Drug Report, 3.9 percent of the global population aged 15-64 (192 million people) used cannabis within the past year (United Nations, 2020). Not surprisingly, past-year cannabis use within the North American subpopulation is substantially higher, coming in at 14.6 percent (United Nations, 2020). Usage rates have continued to rise. We believe this is likely due to the widely accepted, yet false, notion that cannabis is completely safe.

Furthermore, cannabis legalization reforms have swept across the United States in recent decades, perpetuating its social acceptance and availability.

Regardless of the common misconceptions surrounding the relative safety of cannabis, its use can result in severe adverse health effects including, but not limited to, stress cardiomyopathy, myocardial infarction, pulmonary tissue damage, increased occurrences of severe pulmonary infections, and cerebral vascular accidents. Although they are frequently underreported, adverse cardiovascular and pulmonary events are being described at an alarming rate. Surprisingly, it has been found that younger adults have the highest relative risk for experiencing many of the more severe cardiovascular events.

Based on the information found within this literature review, future critical care implications for respiratory therapists should include (1) Δ-9-THC drug screening of patients who are presenting with idiopathic conditions that align with cannabis use, yet have not disclosed using cannabis (potentially due to the misconception of it being completely harmless), (2) advising cardiac patients (chronic, acute or in rehabilitation) of the potentially lethal risks of cannabis use, and (3) educating cannabis users who are suffering from pulmonary conditions such as chronic bronchitis or pneumonia of the known etiology connecting cannabis use and their condition.

**References**


