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Review Article

Surgical considerations of marijuana use in elective procedures

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Abstract

Background: Marijuana consumption is estimated as upwards of 9.5% of the U.S. adult population. Nevertheless, few trials exist on potential implications for surgical outcomes amongst users.

Methods: A current literature review explored marijuana's effects to answer: (I) How is marijuana use screened for in clinical and pre-operative settings? (II) What are potential surgical complications of marijuana use? (III) How should surgeons handle patient marijuana use regarding elective surgery? (IV) Are marijuana's effects the same or different from those of tobacco?

Results: In acute settings, marijuana's effects peaked at approximately 1 hour post initiation, lasting 2–4 hours. Marijuana increased cardiac workload, myocardial infarctions and strokes in young, chronic users. Cannabis caused similar pulmonary complications to those of a tobacco smoker. Marijuana caused airway obstruction and increased anesthetic dosages needed to place laryngeal airways. Use within 72 hours of general anesthesia was advised against. *In vitro* and *in vivo* studies were contradictory regarding prothrombic or antithrombotic effects.

Conclusions: Marijuana use is problematic to surgeons, left without evidence-based approaches. In emergency settings, marijuana use may be unavoidable.

However, further research would provide much needed information to guide elective procedures.

Keywords: Evidence-based medicine, Surgery, Health profession

1. Introduction

Marijuana use dates back to 2727 BC to Chinese Emperor Shen Nung. After spreading through the Greek and Roman empires and into the Islamic empire of North Africa and the Middle East, it was brought to the Western hemisphere by the Spanish [1]. Originally lauded for its utility as fiber, it was not until its migration into North America that it began to be used in a similar fashion as it is today. Used in the form of hemp, it was seen throughout society as rope, clothing and even paper.

While marijuana has been used by Americans recreationally for years, it is a subject that is becoming more commonplace in our modern society. According to the National Institutes of Health, marijuana use in 2015–2016 rose from 4.1% to 9.5% of the U.S. adult population [2]. With more states eliminating the legal ramifications of its use and a growing debate about its federal legality, this is a subject that routinely makes local and national headlines. With a diverse array of commercial products becoming available from chocolate squares to oral sprays, marijuana is also no longer restricted to a rolled cigarette.

The medical community has also joined the debate. The most obvious correlation between medicine and marijuana is medicinal marijuana. Marijuana's effects have been well documented, allowing the push for its use as medicine within multiple specialties. Proponents of its use point to its effects on the endocannabinoid system. Studies show that through its impact on different pathways it may be used as an analgesic, immunosuppressant, muscle relaxant, anti-inflammatory agent, appetite modulator, antidepressant, antiemetic, bronchodilator, neuroleptic, antineoplastic and antiallergen [3]. Medical marijuana also differs in chemical composition, containing a higher tetrahydrocannabinol (THC) concentration and less cannabidiol than the recreational version. This is even before taking into consideration the various extraneous agents that may be found within the available recreational drug [4].

There is however, very little, if any research evaluating marijuana's use in surgery. This paucity of literature presents a problem. While many surgeons may ask about recreation drug use including marijuana, many other drugs have established evidence based outcomes that allow variation in surgical planning as needed. However, when it comes to marijuana, surgeons are left to determine what to do with this information on their own.

Despite the multiple studies on the physiologic effects of marijuana use, clinical studies, if any, are not cited in the medical literature. This study reviews the literature available on marijuana's effects and discusses potential complications that may result within the surgical setting. With a reported estimation of 10%–20% of patients between the ages of 18 and 25 years regularly using marijuana [4], this review seeks to become an initial step for further exploration of the subject and to reveal why there is a need for more in-depth research.

2. Main text

2.1. Methods

2.1.1. Study collection

A search on the effects of marijuana, marijuana and elective surgery, and marijuana's effects on surgery was undertaken in PubMed, Medline, EMBASE, [Google.com](https://www.google.com) and [Scholar.google.com](https://scholar.google.com). Articles were reviewed using the keywords "marijuana," "elective surgery," "surgery," "anesthesia," "complication," "THC," "tobacco" and "cannabis." After removing duplicates, 263 studies resulted. After articles were identified, attention was paid to study design, type, outcomes and publication. The authors independently reviewed titles and abstracts to ascertain relevance to the topic at hand. Authors also searched reference lists of included studies as well as other narrative reviews.

2.1.2. Data consideration

Due to limited research and reviews on this subject, information was utilized from articles on surgery in various fields, such as orthopedic, dental and bariatric with anesthesia considerations and general topics related to marijuana also examined. The following information was gathered: marijuana's prevalence in the United States, marijuana's effects on the cardiovascular system and pulmonary system, potential coagulopathies, marijuana's effects in relation to anesthesiology, evidence based screening methods for recreational drug use, potential surgical complications that may result from marijuana use, and recommendations on marijuana use and surgery.

2.1.3. Analysis

Information pulled from the literature was used to answer the following key questions: (I) How is marijuana use screened for in clinical and pre-operative settings? (II) What are potential complications in the surgical setting of marijuana use? (III) How should surgeons handle patient marijuana use regarding elective surgery? (IV) Are marijuana's effects the same or different from those of tobacco?

2.2. Results

2.2.1. Pharmacological effects

When marijuana is smoked, THC and other cannabinoids are absorbed rapidly through the lungs with effects peaking in 15 minutes. These effects can persist for up to a dose-dependent 4 hours in the acute setting. When ingested orally however, onset of effects is slower (15 minutes versus 90 minutes) but has a longer duration of action (4 hours versus 5–6 hours), due to continued absorption in the gut. This is despite a lower bioavailability due to first-pass metabolism by the liver which results in a blood concentration 25% of what is obtained if smoked. The cognitive/psychomotor effects can be present for up to 24 hours regardless of administration route [4]. Cannabinoids are highly lipid soluble. This leads to a slow release into the bloodstream with a single dose not fully eliminated for up to 30 days [5].

The cardiovascular effects of marijuana use range from benign to worrisome based on the timeline of use and dosage. In a series single blind study comparing the effects of high and low doses of THC in healthy young men, tachycardia was induced beginning within the time of inhalation, and persisting at least 90 minutes, with the maximum heart rate reached at an average of 30 minutes. The study also found a significant elevation in systolic and diastolic blood pressures as well as the presence of premature ventricular contractions (PVCs) in subjects who received the higher doses. These experiments showed a correlation between the dose and the tachycardic and cardiovascular changes [6]. In addition, Malit *et al.*'s study on the effects of intravenous THC found the majority of patients to exceed the 100 beats per minute mark but also experience intermittent spikes in heart rate with a possible etiology of psychological distress [7]. Beaconsfield *et al.* postulated a mechanism of beta adrenergic stimulation for the tachycardia as he was able to block the tachycardia with the use of propranolol [8].

Pharmacology lays credence to this. At lower or moderate doses, marijuana increases sympathetic activity reducing parasympathetics and producing an elevation in heart rate, cardiac output and blood pressure. However, the opposite is true as the dosage increases. At high doses, the parasympathetic system takes over, leading to bradycardia and hypotension with animal studies postulating that the sympathetic inhibition occurs due to the bioactive constituent of cannabis's effects on the CB1 receptors [9].

In addition to sinus tachycardia, marijuana use has been linked to multiple electrocardiogram (ECG) changes in various case reports. Daccarrett *et al.* found Brugada-like changes in a 19 year old male with a known history of cannabis use and no anatomical/functional abnormalities [10]. A case was also reported in which cannabis use was linked to the development of atrial flutter and atrial fibrillation [11], while other studies have reported the presence of sinus bradycardia and AV block [12, 13].

Marijuana use also has a role as a risk factor for myocardial infarction. Aronow *et al.*, found that while comparing marijuana to placebo, cannabis causes an increase in carboxyhemoglobin, a resultant increase in myocardial oxygen demand, decrease in oxygen supply as well as an induction of platelet aggregation [14]. One case report showed a 21 year old male who presented with a ST elevation myocardial infarction due to plaque rupture as a complication of marijuana use [15]. In Mittleman *et al.*'s analysis of over 3,800 cases of myocardial infarction, 124 patients reported use within the last year of which 37 reported use within 24 hours, with 9 reporting use within an hour of the event. The study found a statistically significant 4.8 fold increase in myocardial infarction within the first hour of marijuana use ($P < .001$). In fact, as THC content of marijuana increases, there are a growing number of clinical studies demonstrating the association between cannabis use and adverse cardiovascular events. One such study followed 1913 adults prospectively and demonstrated that in patients with prior myocardial infarction, marijuana use up to once per week increased risk of death 2.5 fold while more frequent use yielded a fourfold risk of dying [16].

Marijuana has also been reported as a risk factor for stroke. Over 80 cases have been reported in which patients had strokes, with a higher prevalence of ischemic strokes, that were associated with either a recent increase, in the days leading up to the event, or chronic history of heavy marijuana use. They believed that the marked swings in blood pressure or the reversible cerebral vasoconstriction that resulted from marijuana use were likely mechanisms of stroke but admitted that no firm conclusions could be drawn without further studies [17]. In addition, Lawson reported a similar belief that drug induced vasospasm was a plausible explanation for TIAs, but also with the caveat that due to the confounding medications/illicit substances being used in his patient, no direct association could be determined [18].

Also of interest is marijuana use's effect on other cardiovascular vessels. When cohort studies were performed comparing marijuana users with resultant limb arteritis to patients suffering from thromboangiitis obliterans, marijuana associated arteritis occurred in younger, usually male patients with a unilateral, lower limb as the common presentation [19].

The most common route of marijuana administration is inhalation via smoking. Due to the unfiltered nature of the marijuana cigarette compared to commercially available tobacco cigarettes, the amount of carcinogens and irritants, like tar, that enter the upper airway is increased [20] with approximately a three-fold increase in tar inhalation and one third more tar deposition in the respiratory tract [21]. More specifically, the tar produced from cannabis smoke contains greater concentration of benzanthracenes and benzopyrenes (each a carcinogen) than tobacco smoke [22]. In addition, as compared to smoking tobacco, there is a two-thirds greater puff volume, one-third greater depth of inhalation and a four-fold longer breath-holding

time, all of which are common practices to try to maximize THC absorption, which is around 50% of cigarette content [21]. These practices result in five times the amount of carboxyhemoglobin levels as compared to the typical tobacco smoker [23] despite the presence of similar quantities of carbon monoxide from the incomplete combustion of the organic compounds found within each product [24]. In reporting his case, Schwartz theorized that high temperatures in which marijuana burns compared to tobacco may increase the irritancy of marijuana to the mucous membranes [25]. While the higher temperature is a possibility, the evidence of marijuana's irritancy is well documented. In a cohort study comprised of 40 healthy patients, Roth *et al.* showed that cannabis smokers had significantly increased visual bronchitis index scores resulting from large airway epithelial damage, edema, and erythema. On mucosal biopsy, goblet cell hyperplasia with subsequent increase in secretions, loss of ciliated epithelium and squamous metaplasia were also present in 97% of smokers. They concluded that marijuana use is associated with airway inflammation that is similar to that of a tobacco smoker [26]. A cross-sectional study on over 6000 patients, from 1988 to 1994, found an increased incidence of chronic bronchitis symptoms such as wheezing and productive cough occurring in patients 10 years younger, on average, than tobacco smokers [27]. Case-control trials performed found similar findings with regards to increases in wheezing, shortness of breath, cough and phlegm as well as the similarities with tobacco use [20].

Bryson also concluded based on his review of the literature, that the pulmonary complications in the chronic marijuana smoker are equivalent to those seen in the chronic tobacco smoker [28], while Wu *et al.* estimated that 3–4 cannabis cigarettes daily equates to about 20 tobacco cigarettes in terms of bronchial tissue damage [21]. Cannabis use has also been linked to a higher risk in cancers, possibly due to the increased carcinogens entering the airway. Similar to tobacco use, marijuana use plays a significant role in the development of lung cancer. In a case control study performed in New Zealand, young adults (under the age of 55) had an 8% increase in lung cancer risk for each joint year of cannabis smoking after adjusting for the cofounders, such as age, sex, ethnicity and family history [29]. Berthiller *et al.* pooled data from a multitude of institutions across multiple countries, comprising of over 1200 patients, and reported an increased risk of lung cancer for every marijuana use [30]. In addition, a 40 year cohort study (1969–2009) with about 48,000 patients reported an increased risk of lung cancer in young men (aged 18–20 years old) who had smoked marijuana more than 50 times. This study was limited however by the nature of patient self-reporting [31]. Head and neck cancers have also been theorized to be at a higher risk similar to that of tobacco smoking. However, a pooled analysis performed by Berthiller *et al.* found that infrequent marijuana smoking did not confer a greater risk after adjusting for cofounders. The authors did note that due to the low prevalence of frequent smoking within the study population, that a moderately increased risk could not be ruled out [32]. In another population based case

control study, there was an increased incidence of head and neck cancers in patients with a 30 joint-year history, yet the association did not exist when accounting for tobacco smoking [33] suggesting the risk is greater with tobacco than marijuana.

2.2.2. *Impact on anesthesia*

Marijuana's prevalence is evident amongst all patient populations. In a cross-sectional study conducted by Mills *et al.*, the rate of marijuana use via patient self-reporting was found to be 14% amongst surgical patients in 2003. This led the authors to conclude that questions about illicit drug use should be a routine part of the preanesthetic assessment, especially in patients that the anesthesiologist finds hard to settle, due to anxiety or other psychologic manifestations, because of the potential anesthetic complications that may occur [34].

In a series of case reports, Guarisco presented three patients who suffered from significant respiratory distress due to isolated uvulitis, a disease of low incidence typically associated with infection or traumatic irritation from instruments used in the airway. Investigating further, all three patients were found to have inhaled large quantities of cannabis within six to twelve hours of the onset of symptoms leading to the conclusion of a possible correlation with inhaled irritants such as cannabis. Due to known cases of isolated uvulitis [35, 36] and the possible link with marijuana, the authors suggest that toxicology urine and blood studies for THC should be performed in cases where marijuana use is suspected but not confirmed by history taking [37]. Multiple other cases have also been reported with similar findings. In a case series by Sloan, three adolescents suffered acute uvular inflammation post the heavy use of marijuana, having smoked at least three marijuana cigarettes, despite negative throat cultures [38]. In 1971, a cohort study was performed in which a large quantity of marijuana, over 100 grams, was smoked over several months. Of the 31 subjects, almost half suffered from recurrent rhinopharyngitis as well as developed acute uvular edema after the heavy marijuana inhalation which lasted approximately 12–24 hours [39]. These findings stress the importance in the maintenance of the airway during anesthesia following acute marijuana use due to the potential airway obstruction that may occur.

In fact, in presenting a case of uvular edema and airway obstruction with cannabis inhalation 4 hours prior to surgery, Pertwee recommended that elective operations should be avoided altogether if a patient was recently exposed to cannabis smoke [40]. This recommendation seems reasonable when taking into consideration the life-threatening bronchospasm leading to asphyxia, brain damage or death resulting from tracheal intubation in patients with obstructive airways [41]. One proposed course of action has been the therapeutic use of steroids. In Guarisco's study, he theorized that steroids should help inhaled irritant uvulitis [37]. As steroids increase endotracheal permeability, decrease mucosal edema and stabilize lysosomal

membranes, thus decreasing the inflammatory response, the theory has scientific basis. In a prospective, randomized, double-blind study, Silvanus *et al.* found that the addition of methylprednisolone to salbutamol in patients with a partially reversible airway obstruction helped in the diminution of the reflex bronchoconstriction that can result from tracheal intubation [42]. This led to Hawkins *et al.*'s recommendation that at the first signs of airway obstruction, dexamethasone should be used as the drug of choice, 1 mg/kg every 6–12 hours over the course of one to two days (Hawkins). This recommendation gained credence in the dramatic relief that dexamethasone provided in the post-traumatic cases [35, 36]. However, Mallat *et al.* concluded that although marijuana-induced uvular edema is a serious postoperative complication that has a potential for simple treatment, in the case of an elective surgical procedure with an acute history of cannabis exposure, surgery should be cancelled as prophylactic treatment may not be efficient [43]. The complications of the airway are not limited to intubation however. The inhalation of toxic chemicals as well as smoke can cause laryngospasm by chemoreceptor stimulation. In addition, the inhalation of hot gasses can trigger laryngospasm via thermoreceptor stimulation, especially in the case of lowered sensory afferent neuron threshold potentials such as in light anesthesia. In line with this, White presented a case in which a known cannabis smoker suffered severe laryngospasm following extubation [44].

As found within the reviews, multiple observations have been made showing cross-tolerance between marijuana and barbiturates, opioids, prostaglandins, chlorpromazine and alcohol. In addition, animal studies have shown additive effects amongst them all except for alcohol [45, 46]. These drug interactions have led to further exploration of its reactions to other medication groups. As a result of fat sequestration and subsequent slow elimination from the tissues, cannabinoids may be present to interact with multiple anesthetic agents. In Symons's case report, the patient required multiple boluses of propofol and two additional doses of midazolam to achieve appropriate sedation [47]. In a prospective, randomized, single-blind study of 60 patients, chronic marijuana users required significantly increased doses of propofol to facilitate successful insertion of the laryngeal mask and thus suggesting that the increased doses, in chronic marijuana users, may be a requirement for appropriate loss of consciousness as well as jaw relaxation and airway reflex depression. The authors theorized that the variations in the level of delta9-THC can explain variations in propofol responses [48]. In a review written in the American Association of Nurse Anesthetists Journal, Dickerson reported the synergistic effects of cannabis to include: potentiation of nondepolarizing muscle relaxants, potentiation of norepinephrine, the augmentation of any drug causing respiratory or cardiac depression, as well as a more profound response to inhaled anesthetics sensitization of the myocardium to catecholamines due to the increased level of epinephrine [49]. On the subject of muscle relaxants, THC depletes acetylcholine stores and exerts an anticholinergic effect and thus creates a potentiation of the nondepolarizing muscle relaxants [50]. A

review by Hall *et al.* explored THC's interaction with drugs affecting heart rate and arterial pressure and found that due to cannabis's own cardiovascular effects (as discussed previously), it may interact with medications such as beta-blockers, anticholinergics and cholinesterase inhibitors [51]. Due to these potential autonomic reactions, as well as theoretical psychiatric complications, such as withdrawal effects and their interference with anesthetic induction or postoperative recovery, there has been a stress made to inquiring about drug history [52, 53] or avoiding elective operations altogether [53]. Dickerson, in his review, recommended that, due to all potential effects and interactions, not only should an extensive history of drug use be elicited at the time of the preoperative assessment, including the frequency of use and time of last use, but that anesthesia should be avoided in any patient with cannabis use within the past 72 hours [49]. This gained further credibility in a randomized, double-blind trial, in which an apparent drug interaction was observed in the patient population who underwent general anesthesia within 72 hours of marijuana use leading to a sustained postoperative tachycardia, a finding potentially due to an interaction between cannabinoil metabolites and atropine administration during anesthesia [54].

2.2.3. Peri-operative complications

One of the most researched and known risk factor for peri- or postoperative complications, increased hospitals costs and resource usage is smoking, specifically tobacco smoke. In fact, the rates of perioperative respiratory events, such as re-intubation, hypoventilation, hypoxemia, laryngospasm, bronchospasm, and aspiration, have a total incidence of 5.5% in smokers compared to 3.1% in nonsmokers, making these events 70% more prevalent with smoking [55]. In addition, in a randomized controlled trial out of Denmark, orthopedic surgery patients who smoked were compared to those who underwent cessation counseling and nicotine replacement therapy. In the study, they found an overall complication rate of 18% compared to the 52% found in the smoking group, including a cardiac event rate of 0% compared to 10% [56]. A similarly designed study found a significant relative risk reduction of 49% for not only systemic complications but that of wounds as well [57]. These call into question the role of marijuana on perioperative complications, especially when taking into consideration that the pulmonary complications in the chronic cannabis smoker are equivalent to that of a chronic tobacco smoker, probably due to the cannabis smoke products [28]. One such pulmonary complication is airway obstruction, extensively linked to marijuana use [35, 36, 37], in which Warner *et al.* found that untreated, such as a lack of smoking cessation in the case of marijuana, leaves patients at a high risk for perioperative complications [58].

When it comes to the case of cardiovascular maintenance in the perioperative period, marijuana presents complications. As mentioned previously, cannabis use can create

a series of ECG changes that must be considered and monitored such as PVCs [6], atrial fibrillation [11], AV block [12, 13], or Brugada-like changes [10]. As a worst case scenario, cannabis use has been linked to plaque rupture and resultant myocardial infarction [15]. These are all causes for concern considering that Gregg *et al.* reported, in conducting a series of 55 clinical trials in patients medicated with THC, that peak heart rate increased by 24.1% in surgical patients compared to the non-surgical. The authors concluded that THC may have a synergistic cardiovascular relationship with surgical stress [54]. This tachycardia gave credence to Bryson's recommendation that ketamine, pancuronium, atropine and epinephrine, all drugs known to affect heart rate, should be avoided in patients with history of acute marijuana use [28], while the bradycardia and hypotension that results from high doses of marijuana called into question the amount of atropine and vasopressors needed [9]. Despite the impetus behind these recommendations, 1 trial showed epinephrine to have no synergistic effect with marijuana when it comes to cardiovascular effects [54], showing more research is needed on the potential interactions of marijuana and perioperative medications.

Field visualization plays a key role in any operation. Marijuana, however, may affect this. In a literature review published in Poland, Zakrzeska *et al.* explored how cannabinoids and their metabolites and their effects on the receptors CB1, CB2, CBPT and CBED as well as other systems may impact hemostasis. The authors concluded that despite the studies that have shown contradictory effects, based on the physiology, it is reasonable to conclude that marijuana could have an anti-hemostatic effect [59]. Multiple studies have backed up that conclusion. In 1979, Schaeffer *et al.* reported that cannabis users had a diminished ability for platelet aggregation [60]. This led to further investigations and in 1989, Formukong *et al.* looked at cannabinoids' effect on platelet aggregation. The authors found that in both rabbit and human platelet aggregation that was induced by adenosine diphosphate or epinephrine was inhibited by cannabinoids in a dose-dependent manner and with cannabidiol more potent than THC in this effect [61]. Then in 2007, an *in vitro* coagulation study showed that marijuana and two of the major cannabinoids, including THC, had an anticoagulant property and even more so, an antithrombotic effect. In the *in vivo* model testing clotting times of lean and obese rats, those treated with cannabis had clotting times 1.5 to 2 times greater than the controls, thus supporting the results of the *in vitro* study [62]. In a follow-up study in 2014, the whole blood of donors who had consumed cannabis had diminished platelet aggregation. The conclusion was drawn that endocannabinoid receptor agonists reduce platelet activation as well as aggregation, and as such might have potential in antithrombotic therapies [63]. This anticoagulatory effect could counteract the surgeon's attempts to create hemostasis within the operative field and thus limit visualization.

Yet Zakrzeska also concluded that marijuana use may put certain individuals at risk for thromboembolism [59], a second issue of surgical concern. Even though an

intravenous injection of cannabis has been shown to cause a significant drop in the platelet count which seems in line with the belief of anticoagulation, it is the marijuana components that cause a release of ADP from erythrocyte, leading to platelet aggregation. This aggregation is the reason behind the reduction in platelet count [64]. The theory of marijuana use leading to platelet aggregation leads toward substantiating the conclusion Desbois *et al.* made in regards to an increased predilection for myocardial infarctions and arterial disease [19]. Reports of cases similar lead to Deusch *et al.*'s *in vitro* study. The cannabinoid receptors CB1 and CB2 were found on the cell membrane of the human platelet via western blot. Delta-9-tetrahydrocannabinol, which is the ingredient within cannabis responsible for the psychological effects, demonstrated the ability to significantly increase the expression of glycoprotein IIb-IIIa as well as P-selectin thus increasing the activation of the human platelet. This findings lead to the conclusion that THC, through its effects on the cannabinoid receptors on platelets, may create a prothrombotic setting favoring the development of cardiovascular events [65].

As surgical technique and field advance, more complicated and potentially painful procedures are becoming more common practice. Surveying patients indicated that over 80% experience postoperative pain that was rated as either moderate or severe [66]. This pain can set off a series of physiologic changes that may harm various systems ranging from cardiovascular to the central nervous system [67], and has been shown to lengthen hospital stays and time to first ambulation, impede postoperative nursing and physiotherapy, increase healthcare costs, and reduce the patient's satisfaction with the outcome [67]. However, multiple reviews of the available literature have concluded that appropriate and adequate postoperative analgesia improves recovery, including improving cardiac function and decreasing mortality and morbidity related to pulmonary function, decreases thrombosis risk, diminishes the possibility of chronic pain syndrome, and improves overall outcome [68]. Marijuana plays a role now in medicine as an analgesic. Prescribed for a number of diagnoses, medical marijuana has been shown in over 18 randomized trials to be both effective and safe in the treatment of chronic pain, with the best evidence being for neuropathic pain [69]. Investigating the role marijuana plays as an analgesic, Russo found that due to cannabis's role in multiple pathways, safety, and potential side effects and benefits shown in the clinical trials, marijuana may play a more important role in pain management when combined with opioids [70]. However, the appropriate management of marijuana users with opioids postoperatively is more complicated than these trials suggest. In chronic marijuana users, the perioperative narcotic requirements to gain appropriate analgesia were significantly increased. Yet despite this increase, patients were more likely to subjectively experience less pain than those of their non-marijuana using counterparts [71]. Clinically, this increase materialized in the form of a narcotic requirement twice that of the average patient of the same height and weight each day over the course of two

postoperative days [50], demonstrating a potential interaction between marijuana and opioids which must be taken into account when considering the potential postoperative complications that may arise from the increased doses of opioids.

In a literature review published in the *Journal of Obesity Surgery*, Rummel *et al.* posed the question of whether or not marijuana use should be a contraindication to bariatric surgery. In their investigation, the authors determined that there was a lack of a generalized screening protocol for marijuana use amongst providers and thus there is no account of a known effect on procedures due to confounders. Yet, due to the many effects marijuana has on the cardiovascular, pulmonary, immunologic, and central nervous system, the conclusion was drawn that it is fair to hypothesize that cannabis use has the potential to worsen adverse outcomes in the postoperative period [72]. These potential risks and lack of screening resulted in the recommendation that practitioners of bariatric surgery should be devoted to assessing controlled and problematic levels of preoperative substance use and take the time to discuss the potential postoperative risks with patients [73]. However, the American Association of Clinical Endocrinologists, the Obesity Society, and the American Society for Metabolic and Bariatric Surgery took the recommendations one step further by stating that current drug use, including marijuana, should be treated as exclusionary criterion in the case of bariatric surgery [74]. These recommendations for an elective procedure should potentially be considered in the case of all elective surgical procedures.

3. Conclusions

After an extensive and comprehensive review of available literature, a fund of knowledge was found to exist pertaining to the physiological effects of marijuana as well as the metabolites within, most notably THC and cannabinol. While this information has been present with 40 years of research, no investigation has taken place pertaining to patients' marijuana use and surgical considerations, such as effect on wound healing, that the piecing together of this data warrants.

The documented evidence of marijuana's effects is of great concern for surgery. Whether it be the presentation of arrhythmias [10, 11, 12, 13], myocardial infarction [15, 16], stroke [17], pulmonary obstruction [35, 36, 37] as well as anesthetic concerns [47, 48, 50] and/or thromboembolus [19, 64, 65] or bleeding [59, 60, 61, 62, 63], marijuana's multi-system, multi-organ effects are possible confounders to a variety of medical outcomes, let alone surgical. With THC and cannabinoids being shown to be present for up to 30 days within the fat [5], its potential to affect the entire operative course in either chronic or acute smokers must be evaluated.

One potential reason behind the lack of or limitation of clinical trials pertaining to surgical outcomes, including wound cleaning, is due to the most commonly smoked

drug, tobacco. While this may change in time with marijuana use being legalized in more states and the potential increase in patients admitting use, the available clinical trials and cohort studies suffer from the current difficulties. As there is a relationship between the smokers of tobacco and those of marijuana, it can also be difficult to separate out the effects of one from the other. While the marijuana cigarette may contain more carcinogens [20, 22] and equate to more tobacco cigarettes in number [21], the resultant airway inflammation is similar to that of tobacco [26], blurring the causation line via pathologic examination. Additionally, few studies have elicited information on the frequency of use of both marijuana and tobacco products as well as the differences in amount despite the repetition that exists in the recommendations for marijuana screening. However, one particular cohort study of just over 1000 patients was able to separate out the individual acute effects but also the synergistic effects of tobacco use and marijuana use on the lungs via the use of salbutamol and incentive spirometry. This study, however, is limited due to relying on patient self-reporting of lifetime marijuana use [75].

Another possible reason complicating the clinical data on marijuana is the presence of contradictory reports and trials, most prevalent in the debate on coagulopathy [59, 60, 61, 62, 63, 64, 65].

As cannabis use becomes more prevalent within our society due to the legalization of both medicinal and recreational cannabis across the country, the lack of data leaves surgeons without much evidence-based approaches to marijuana management within the surgical patient population, one in which marijuana users comprise 14% of as of 2003 [34]. While a patient's history of marijuana use may be unavoidable in the case of emergency surgery, further research is necessary to provide the needed information to utilize in the time of elective surgical procedures.

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