

## Recreational Marijuana Use: Is it Safe for Your Patient?

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Marijuana is a very old drug with documented use reaching back to Chinese emperors and Egyptian pharaohs. Ancient civilizations described the medicinal value of marijuana, promoting it for its healing powers, anti-inflammatory properties, and as a treatment for many different disease states.<sup>1</sup> In the several intervening millennia, the medicinal claims surrounding marijuana use have been validated in many cases, and therapeutic benefits have been described for a variety of medical conditions.<sup>2–4</sup> Today medicinal marijuana plays an important role in the management of chronic neuropathic pain, glaucoma, multiple sclerosis, HIV, and other conditions associated with chronic pain.<sup>4</sup> In light of clinical evidence in support of medical marijuana, a number of countries as well as 20 individual states and the District of Columbia in the United States have legalized marijuana for medicinal purposes. Interestingly, legalization was extended to include recreational use in the states of Colorado and Washington, with additional referendums pending in several other states including Alaska, Arizona, Maine, Missouri, Montana, Oregon, and Wyoming.<sup>5</sup>

While the role of medical marijuana is indisputable in patients suffering from chronic, debilitating pain, the potential for widespread legalization of marijuana for recreational purposes raises important questions regarding safety. For example, do we really know enough about the cardiovascular effects of marijuana to feel comfortable about its use in patients with known cardiovascular disease or patients with cardiovascular risk factors? As early as 1972, Beaconsfield

et al<sup>6</sup> showed that marijuana smoking resulted in tachycardia. A decade later, the surgeon general of the United States issued a warning on the use of marijuana, describing it as a major public health problem, based on findings that marijuana consumption leads to a variety of cognitive, behavioral, and other systemic problems including respiratory, reproductive, and immunological disturbances.<sup>7</sup> Here, we will focus on the cardiovascular effects of marijuana and the implications for recreational use.

We recently reviewed reports in the literature that described a temporal association between marijuana use and serious cardiovascular events (Table).<sup>8</sup> Several instances of temporal association between marijuana use and myocardial infarction were reported in the literature. In cases where marijuana use was linked to myocardial infarction, patients tended to be younger and have no other risk factors for infarction.<sup>9</sup> The 2006 CARDIA study showed that marijuana use is associated with hypertension, dyslipidemia, and higher caloric intake, all of which may increase the incidence of coronary artery disease.<sup>10</sup> In light of the probable effects of marijuana on increasing platelet coagulability<sup>11</sup> and its frequent combined use with smoking tobacco or other illicit drugs, it is not surprising to note these reports of myocardial infarctions. In a review of 3882 patient interviews, Mittleman et al<sup>12</sup> found a significant 4.8-fold increase in the incidence of myocardial infarction over baseline in the first hour after marijuana use. Similarly, a 4.2-fold increase in mortality rate was observed in marijuana users compared with nonusers following myocardial infarction.<sup>13</sup>

There is some suggestion that heavy marijuana use may lead to no-reflow phenomenon in both the heart and brain, implying an effect on small vessels and arterioles.<sup>14,15</sup> In addition to myocardial infarction, marijuana use has also been temporally related to cardiac arrhythmia,<sup>14,16</sup> cardiomyopathy,<sup>17</sup> and arteritis.<sup>18</sup> Similarly, several reports of cerebrovascular events have been described in association with marijuana inhalation ranging from transient ischemic events to strokes.<sup>19</sup> The most striking feature of these events is incidence in very young patients with no other risk factors. No-reflow or cerebral artery spasm has been implicated, but the exact mechanism is not well established. Regardless of the mechanism, the evidence in the literature suggested to us

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**Table.** Summary of the Major Cardiovascular and Cerebrovascular Adverse Effects Temporally Related to Marijuana Inhalation

Cardiovascular	Peripheral	Cerebrovascular
Increased angina Myocardial infarction Coronary no-reflow Cardiac arrhythmias Cardiomyopathy	Raynaud's phenomenon Ischemic ulcer Digital necrosis Angitis	Transient ischemic attacks Cerebral no-reflow Stroke

that a mandate to report the cardiovascular effects to state health authorities, such as that described in the current issue of *JAHA* by Jouanjus et al,<sup>20</sup> may be a reasonable strategy for gathering additional safety data, and we applaud Jouanjus and colleagues for bringing this model of active surveillance to international attention.

In this issue of *JAHA*, Jouanjus et al report on cardiovascular complications of marijuana use reported to the French Addictovigilance Network, a nationwide network of regional Addictovigilance centers focused on achieving reliable surveillance of abuse and pharmacodependence cases.<sup>20</sup> This report suggests that the plethora of single case reports describing temporal association between acute coronary syndromes and other cardiovascular events and marijuana use are more than just coincidence.<sup>8</sup> From 2006 to 2010, ≈2% of cannabis-related reports to Addictovigilance were of cardiovascular complications. In addition, the incidence of cardiovascular complications appears to be on the rise, increasing from 1.1% of all cannabis-related incidents in 2006 to 3.6% in 2010. Perhaps most disturbing is the mortality rate of 25% in cases of cannabis-related cardiovascular complications. While the concomitant use of other products, such as tobacco and alcohol, may have contributed to some of these events, approximately half of the patients who presented with cardiac events had a record of exposure only to marijuana.<sup>20</sup>

As the authors point out, this type of study has limitations.<sup>20</sup> For example, we really do not know what the denominator is, and it is likely that cardiovascular events related to cannabis use were under-reported due to an unwillingness to disclose information regarding illicit drug use in the emergency department and to attend the emergency department when under the influence. Nevertheless, this paper does suggest a signal linking cannabis use to cardiovascular events and is deserving of our attention, underscoring the need for more research in this field.

As described above, there is considerable evidence to suggest a therapeutic benefit of inhaled marijuana for a variety of medical conditions.<sup>2-4</sup> As with other medically indicated drugs, use of medical marijuana must be undertaken with cautious consideration of both the benefits and side effects of treatment. However, the perception that

marijuana is safe is deep-seated in the public and even amongst some health professionals. As such, strong lobbying groups are now working to legalize marijuana for recreational use with success to date in 2 states. Use of marijuana for recreational purposes represents a challenge distinct from that of medical use. We believe the time has come to stop and think about the best way to protect our communities from the potential danger of widespread marijuana use in the absence of safety studies. It is understood that randomized controlled trials designed to study the safety of marijuana would be difficult or even unethical. However, the French Addictovigilance Network described by Jouanjus et al offers a reasonable model.<sup>20</sup> We suggest adoption of a similar system for mandatory reporting of the medical complications of marijuana use in the United States. Emergency department providers need to specifically ask patients who present with cardiovascular events about drug use, just like they inquire about tobacco use and other cardiovascular risk factors. It will be especially important to determine whether there are increases in visits to emergency rooms and hospital admissions for cardiovascular events temporally related to cannabis use in those states that have approved the recreational use of marijuana. In addition, there is a need to better understand the true effect of marijuana, both acute and chronic, in basic science models of the normal and diseased heart.

In summary, there is clear clinical evidence to suggest a therapeutic benefit of inhaled marijuana for the management of a number of chronic, debilitating conditions. However, clinical evidence also suggests the potential for serious cardiovascular risks associated with marijuana use, including myocardial infarction, serious cardiac arrhythmias, stroke, and even death.<sup>7</sup> This has been shown repeatedly in case reports, retrospective studies, and registries and is once again demonstrated by data captured by the French Addictovigilance Network.<sup>20</sup> We strongly suggest a national system for mandatory reporting of medical complications related to marijuana use. It is the responsibility of the medical community to determine the safety of the drug before it is widely legalized for recreational use. It is also important to educate health care providers and the public of the potential risk of developing a cardiovascular event associated with the use of marijuana.

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## Disclosures

None.

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