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Editorial commentary: Cardiovascular complications of cannabis use^{☆,☆☆}



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Cannabis use has recently increased sharply and is currently being used by the highest number of users worldwide. According to an estimate, ten million users were added in the year 2016 only [1]. The various States in the United States and Canada have legalized recreational use of cannabis, which has largely contributed to the rise of its users' base. Continued evolution of this change in the legalization process across the world will further contribute to the increase in the use of cannabis. Cannabis use, which was made illegal at the beginning of the twentieth century, is quickly regaining its status of a legal and possibly a natural product since the early 2010s. Its representation as "Medical Marijuana" for the prescription medicine has noticeably made an impact on the mindset of the general public. Now, cannabis is firmly believed to be potentially beneficial in a wide range of symptoms and disease states, and communication through popular media has contributed to the widespread dissemination of this general belief. Although these beliefs rely on relatively modest scientific evidence, its benefits are rarely questioned, even by a part of the scientific and medical communities who besides usually claims for evidence-based medicine.

Rezkalla and Kloner [2] introduce their review article "Cardiovascular Effects of Marijuana" in Trends in Cardiovascular Medicine with a useful reminder that both benefits and risks of cannabis are required to be further examined. The authors present a balanced opinion depending on the therapeutic or recreational natures of cannabis use, but safety concerns are also raised depending on the context and motivations for the purpose. In the United States where both types of cannabis use are authorized in many parts of the country, recreational use of cannabis is almost systematic in the people who use it for medical purposes. In contrast to the generally recognized benefits, the potentially related health consequences often remain secondary. Some clinical trials have evaluated the potential efficacy of cannabis-based products but have also failed to identify the signals of specific adverse events possibly due to the low number of participants. Indeed, the median number of participants was of only 40 per trials according to the meta-analysis performed by Stockings and colleagues in 2018 [3]. Moreover, the rate of withdrawal due to the adverse events was

three-fold higher in the treatment group as compared to the placebo group. In its 2016 report, the World Health Organization (WHO) highlighted the potential health risks of nonmedical cannabis use, including a focus on cardiovascular disorders [4]. The WHO sought more research aiming at understanding the association between cannabis smoking and cardiovascular disease, especially in young adults.

The article by Rezkalla and Kloner [2] presents an updated perspective of previous findings from reviews using a systematic approach [5,6] as it provides a non-exhaustive but representative synthesis of the data published in the scientific literature on various cardiovascular effects of cannabis and cannabinoids. Interestingly, this synthesis includes a detailed description of cardiac dysrhythmias, coronary artery disease (CAD), stroke and other peripheral vascular effects. Some of these disorders are discussed mainly based on the case reports, notwithstanding that these latter are likely to be submitted to significant reducing biases. It is indeed complicated to associate a clinical feature to the use of cannabis, especially in areas where this use is illegal. Also, even when a link is established, many cases remain unpublished. So, the number of cases described in this article, which seems very low compared with the high prevalence of cannabis use, is a substantial underestimation of the real amount of cases.

Nevertheless, the observations described in these clinical cases are confirmed in quality on a broader scale by epidemiological studies measuring the potential association between the cannabis use and different cardiovascular disorders: CAD and ischemic stroke. A significant association was found despite an adjustment on confounding factors including tobacco smoking, which is, as the authors remind us, very often used concomitantly with cannabis. As in previous studies, their findings highlight several striking elements including the young age of the concerned subjects and the absence of known cardiovascular risk factors.

In their article, Rezkalla and Kloner [2] refer to the experience of the French Addictovigilance Network (FAN) specialized in the identification of Addiction signals. The term 'Addictovigilance' corresponds to the safety monitoring of substances (whether licit or illicit) with abuse potential, in the context of real life. From the beginning of the 1990s, this system has progressively implemented a multisource approach combining corresponding data from actors involved in the different aspects of the management of patients with substance use disorders [7]. In the example of cannabis-related events, spontaneous reports, toxicological data, and hos-

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pital records have been explored leading to the identification of signals of increased risk of cardiovascular disorders [8,9]. More recently, this method was refined to improve the efficiency in the identification of somatic disorders related to the use of cannabis and other substances [10]. In 2018, the American Food and drug administration (FDA) explained the usefulness of a similar multi-component approach to comprehending substance abuse matters [11]. Based on the FAN's experience, Rezkalla and Kloner [2] further propose to implement in the United States a systematic program aimed at collecting cardiovascular events in the context of cannabis use. The French model has, indeed, proven to be efficient and would deserve to be promoted elsewhere.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.tcm.2018.12.002](https://doi.org/10.1016/j.tcm.2018.12.002).

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