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PII: S2772-963X(25)00115-2

DOI: https://doi.org/10.1016/j.jacadv.2025.101698

Reference: JACADV 101698

To appear in: *JACC: Advances*

Received Date: 12 January 2025

Revised Date: 4 March 2025

Accepted Date: 6 March 2025

Please cite this article as: Kamel I, Mahmoud AK, Twayana AR, Younes AM, Horn B, Dietzius H, Myocardial Infarction and Cardiovascular Risks Associated with Cannabis Use: A Multicenter Retrospective Study, *JACC: Advances* (2025), doi: https://doi.org/10.1016/j.jacadv.2025.101698.

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Word Count: 1179

Running Title: Cannabis Use and Risk of Myocardial Infarction

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Authors Disclosure: All authors have nothing to disclose

Funding: All authors have no fund

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Introduction

Cannabis use has risen globally due to expanding legalization and social acceptance, with over 192 million users reported by the United Nations in 2018 (1). While it has therapeutic benefits, cannabis consumption has been linked to adverse cardiovascular outcomes, especially myocardial infarction (MI) (1,2).

Research consistently shows a significant association between cannabis use and acute coronary events, particularly among younger users (1). However, confounding factors like tobacco or established cardiovascular risk factors limit the understanding of cannabis' long-term effects (1,2,3). This study aimed to evaluate the long-term cardiovascular effects of cannabis use in relatively healthy individuals.

Methods

Data Source: This retrospective cohort study utilized the TriNetX health research network, which aggregates de-identified electronic medical records from healthcare organizations worldwide. The specific network used for this study was Research, which contains data from 53 healthcare organizations (HCO) throughout the United States. Given the nature of the study and included date, IRB approval was waived.

Study Population: Focused on adults aged ≤50 years between 2010 and 2018, divided into two cohorts. 1) The cannabis-user group with cannabis use diagnoses (ICD-10: F12.1, F12.9, F12.90). 2) The non-cannabis-user group. Both cohorts were free of significant comorbidities at baseline, including hypertension, hyperlipidemia or LDL>100 mg/dL, coronary artery disease including prior MI or history of coronary interventions, diabetes mellitus (DM) or HbA1c >7,

and tobacco use. The relatively healthy status of these patients was a key aspect of this study design, ensuring that comparisons were not influenced by pre-existing high-risk conditions. Propensity score matching (PSM) was performed, covariates were matched by 1:1 PSM using the greedy nearest neighbor matching algorithm with a cutoff of 0.1 pooled standardized mean difference (SMD). The following covariates were included in the PSM: age at index, sex, race, chronic kidney disease, depressive episode (DD), family history of ischemic heart disease, pregnancy, cancer history, creatinine, LDL, HbA1c, BMI, systolic blood pressure.

Study Outcome: The primary outcome included MI defined using ICD-10 codes. Secondary outcomes contained the Major Adverse Cardiovascular Events (MACE) (ischemic stroke, coronary revascularization, and ventricular fibrillation/tachycardia), all-cause mortality, heart failure (HF) and ischemic stroke. The index event was defined as the first-time cannabis use diagnosis was detected and for the non-user group was the first office visit.

Statistical analysis: The analysis was performed with TriNetX Live built-in analytics. Continuous variables were expressed as mean ± SD or median (IQR), and categorical variables were presented as number (%) where appropriate. Baseline characteristics between the 2 groups were compared by using independent t-tests and chi-square tests for continuous and categorical variables respectively. Kaplan-Meier (KM) survival analysis was conducted to demonstrate the survival probabilities difference between the two groups, with statistical significance assessed using log-rank tests. Cox proportional hazards and logistic regression models were used to estimate hazard ratios (HRs) and odds ratio (OR) with 95% confidence intervals (CIs). The significance threshold was established at $P < 0.05$.

Results

A total of 4,636,628 relatively healthy adults aged ≤50 years: 93,267 (2.01%) cannabis-users and 4,543,361 (97.99%) non-users. Cannabis-users were older (26 ± 8 vs 21 ± 9.5 years, P < 0.0001) and had higher comorbidities, including a nearly 15-fold higher prevalence of DD (30.63% vs 1.88%, P < 0.01) and BMI >30 (18.72% vs 3.25%, P < 0.0001). After PSM, each group had 89,776 patients with balanced demographics and baseline health characteristics.

Over 5-years, mean follow-up was 35.7±23.4 months for cannabis-users and 44.2±23.8 months for non-users. MI absolute risk (AR) was 0.558% in cannabis-users vs. 0.09% in non-users, with a risk difference (RD) of 0.468% (95% CI: 0.415%-0.52%), a risk ratio (RR) of 6.185 (95% CI: 4.892-7.82), and an OR of 6.214 (95% CI: 4.913-7.86). KM analysis showed lower survival probability in cannabis-users (99.119% vs. 99.867%, p < 0.0001), with an HR of 7.568 (95% CI: 5.982-9.575).

For ischemic stroke, the AR was 0.405% in cannabis-users vs. 0.094% in non-users, with an RD of 0.312% (95% CI: 0.266%-0.358%), an RR of 4.333 (95% CI: 3.419-5.493), and an OR of 4.347 (95% CI: 3.428-5.512). KM survival probability was 99.395% in cannabis-users vs. 99.866% in non-users (p < 0.0001), with an HR of 5.151 (95% CI: 4.060-6.534).

Regarding MACE, AR was 1.187% vs. 0.366%, with an RD of 0.821% (95% CI: 0.74%-0.90%), an RR of 3.24 (95% CI: 2.864-3.665), and an OR of 3.267 (95% CI: 2.886-3.698). KM survival was 98.2% vs. 99.495% (p < 0.0001), with an HR of 3.869 (95% CI: 3.42-4.38).

For HF, AR was 0.861% vs.0.424%, with an RD of 0.437% (95% CI: 0.363%-0.511%), an RR of 2.029 (95% CI: 1.795-2.293), and an OR of 2.038 (95% CI: 1.802-2.305). KM survival was 98.763% vs. 99.453% (p < 0.0001), with an HR of 2.323 (95% CI: 2.054-2.627).

Regarding all-cause mortality, AR was 1.262% vs. 0.841%, with an RD of 0.421% (95% CI: 0.327%-0.515%), an RR of 1.501 (95% CI: 1.369-1.645), and an OR of 1.507 (95% CI: 1.374-1.653). KM survival was 97.96% vs. 98.86% ($p < 0.0001$), with an HR of 1.813 (95% CI: 1.653-1.989) (Figure 1).

Discussion

This analysis provides evidence linking cannabis-use to adverse cardiovascular events, including MI, ischemic stroke, HF and mortality. Notably, cannabis use appears to pose a substantial and independent risk for these outcomes, even in a population without traditional cardiovascular risk factors. These findings suggest cannabis as a novel and underrecognized risk factor for cardiovascular diseases.

Our study results are consistent with prior research documenting acute coronary syndrome following cannabis use (4). Studies suggest that cannabis use can precipitate MI, particularly within an hour of consumption, with the risk increasing nearly fivefold (1). This effect is pronounced in young, healthy individuals, who present with chest pain (1,5). Cannabis has also been implicated in endothelial dysfunction, pro-inflammatory cytokine release, and oxidative stress, all of which contribute to coronary microvascular dysfunction and plaque destabilization (1,2).

This study has limitations due to lack of detailed cannabis consumption data and potential misclassification. The inherent limitations of real-world data often result from inconsistent patient reporting in electronic medical records. Future research should investigate the dose-response relationship, and the effects of synthetic cannabinoids.

In conclusion, the findings underscore significant cardiovascular risks associated with cannabis use, reinforcing the need for public health initiatives and heightened clinician awareness.

Figure 1: Odds ratios with 95% confidence intervals for cardiovascular outcomes in cannabis-users compared to non-users.

References

1. Jouanjus E, Raymond V, Lapeyre-Mestre M, Wolff V. What is the Current Knowledge About the Cardiovascular Risk for Users of Cannabis-Based Products? A Systematic Review. Curr Atheroscler Rep 2017;19:26.
2. Thomas G, Kloner RA, Rezkalla S. Adverse cardiovascular, cerebrovascular, and peripheral vascular effects of marijuana inhalation: what cardiologists need to know. Am J Cardiol 2014;113:187-90.
3. Moore TH, Zammit S, Lingford-Hughes A et al. Cannabis use and risk of psychotic or affective mental health outcomes: a systematic review. Lancet 2007;370:319-28.
4. Ramphul K, Kumar N, Dhaliwal JS et al. Prevalence of cannabis consumption among acute myocardial infarction patients across various age categories over a two-decade span in the United States. Curr Probl Cardiol 2024;49:102555.
5. Sagris M, Antonopoulos AS, Theofilis P et al. Risk factors profile of young and older patients with myocardial infarction. Cardiovasc Res 2022;118:2281-2292.