Published in final edited form as:
Am Heart J. 2008 March ; 155(3): 465–470.

An Exploratory Prospective Study of Marijuana Use and Mortality Following Acute Myocardial Infarction

Kenneth J. Mukamal, MD, MPH, MA[*], **Malcolm Maclure, ScD**[†], **James E. Muller, MD**[‡], and **Murray A. Mittleman, MD, DrPH**[†,‖]

[*]*Divisions of General Medicine and Primary Care, Beth Israel Deaconess Medical Center, Boston, MA*

‖*Division of Cardiology, Beth Israel Deaconess Medical Center, Boston, MA*

†*Department of Epidemiology, Harvard School of Public Heath, Boston, MA*

‡*Division of Cardiology, Massachusetts General Hospital, Boston, MA*

Abstract

Background—The relationship of marijuana use with coronary heart disease, including prognosis among patients with coronary heart disease, is uncertain.

Methods—We conducted an inception cohort study of 1913 adults hospitalized with myocardial infarction at 45 US hospitals between 1989 and 1994, with a median follow-up of 3.8 years. We ascertained total mortality according to self-reported marijuana use in the preceding year.

Results—A total of 52 patients reported marijuana use during the prior year, and 317 patients died during follow-up. Compared with non-use, marijuana use less than weekly was associated with a hazard ratio of 2.5 (95% confidence interval [CI], 0.9−7.3). The corresponding hazard ratio for use weekly or more was 4.2 (95% CI, 1.2−14.3). The age- and sex-adjusted hazard ratios associated with any use were 1.9 (95% CI, 0.6−6.3) for cardiovascular mortality and 4.9 (95% CI, 1.6−14.7) for non-cardiovascular mortality. In a comparison of 42 marijuana users and 42 other patients matched on propensity scores, there were six deaths among marijuana users and one among non-users (log-rank p = 0.06).

Conclusions—These preliminary results suggest possible hazards of marijuana for patients who survive acute myocardial infarction. Although marijuana use has not been associated with mortality in other populations, it may pose particular risk for susceptible individuals with coronary heart disease.

Introduction

Marijuana use is not uncommon in the United States. A 2001−2002 national survey found that 4.1% of the adult population of the U.S. had used marijuana within the last year.[1] Although younger adults were most likely to report marijuana use, such use among adults aged 45 to 64 years was almost three-fold higher than it had been a decade earlier.

Address for Correspondence: Kenneth J. Mukamal, MD, MPH, MA Division of General Medicine and Primary Care Beth Israel Deaconess Medical Center 1309 Beacon Street, 2nd Floor Brookline, MA 02446 Telephone: (617) 754−1401 Facsimile: (617) 754−1440 E-mail: kmukamal@bidmc.harvard.edu.

Few studies have documented the long-term outcomes of marijuana users. In one previous study of marijuana use and mortality in the general population,[2] Sidney and colleagues found no increased risk of mortality associated with marijuana use among Kaiser Permanente enrollees younger than 50 years of age, very similar to earlier findings among Swedish conscripts.[3] However, marijuana use has cardiovascular effects that could pose particular risk for older adults and those with coronary heart disease, including a sizable increase in resting heart rate.[4] Moreover, in a previous analysis of the Determinants of Myocardial Infarction Onset Study (the Onset Study), the risk of triggering a myocardial infarction was elevated almost five-fold within 1 hour after smoking marijuana, compared with periods of nonuse,[5] consistent with case reports describing this phenomenon.[6-10] However, Steffens and colleagues recently found that orally administered tetrahydrocannabinol, a cannabinoid derivative, inhibits atherosclerosis progression in a mouse model, apparently through effects on lymphoid and myeloid cells.[11] Marijuana use also has a wide variety of non-cardiovascular effects, including potentially adverse respiratory, neurological, and immunological effects.[12-14] The net balance of these apparently disparate effects of marijuana use on the most clinically vulnerable patients, such as those with established coronary heart disease, has not been studied.

An impediment to understanding the clinical consequences of marijuana use has been the stark dearth of studies that have collected information on exposure.[2, 3, 15] To address this paucity of information, we explored the association of marijuana use assessed at the time of acute myocardial infarction with subsequent mortality among participants of the Onset Study. This multicenter, prospective cohort study included chart reviews and in-depth personal interviews with hospitalized patients with confirmed acute myocardial infarction.[16, 17]

Methods

Onset Study Enrollment and Data Collection

The Onset Study was conducted in 45 community and tertiary care medical centers. Between August 1989 and September 1994, 1935 patients (601 women and 1334 men) were interviewed a median of four days after sustaining a myocardial infarction. Trained research interviewers identified eligible patients by reviewing coronary care unit admission logs and patient charts. For inclusion, patients were required to have a creatine kinase level above the upper limit of normal for each center, positive MB isoenzymes, an identifiable onset of symptoms of infarction, and the ability to complete a structured interview. For these analyses, we excluded patients with missing information about marijuana use (n=22), leaving us 1913 eligible patients for analysis. The institutional review board of each center approved this protocol, and each participant gave informed consent; the Beth Israel Deaconess Medical Center Committee on Clinical Investigations gave subsequent approval for linkage to publicly available mortality records.

Trained interviewers used a structured data abstraction and questionnaire form that queried about a range of possible triggers of myocardial infarction, including caffeine, alcohol, smoking, exertion, and anger.[16-20] As part of the interview, participants were asked, “Have you used marijuana, cocaine or amphetamines in the past year,” “how often do you use it,” and “when did you last use it?”

Other information collected from each interview and chart review included patient age, sex, marital status, educational attainment, medical history, and medication use (both prescription and non-prescription). During the chart review, interviewers recorded complications of congestive heart failure or ventricular arrhythmias based upon clinical diagnoses documented in the medical record. Interviewers also collected initial blood pressure on admission and all creatine kinase values available at the time of chart review (median=4).

We defined initial hypotension as a presenting systolic blood pressure of <90 mmHg. We defined current aspirin use as the reported use of any aspirin or aspirin-containing product in the four days prior to the index myocardial infarction. We used 1990 U.S. census data to derive median household income from U.S. Postal Service zip codes. We derived body-mass index from self-reported height and weight. We defined noncardiac comorbidity as any diagnosis of cancer, respiratory disease, renal failure, or stroke recorded in the medical record. Alcohol consumption was assessed with quantity/frequency items for beer, wine, and liquor, which were summed to yield average intake.[17] Tea and coffee intake were assessed similarly.[18] Binge drinking was assessed as intake of 3 or more drinks in a two-hour period within the last year.[21] Physical activity was assessed with a validated inventory derived for this study.[16]

We searched the National Death Index for deaths of Onset Study participants through January 1, 1996 and requested death certificates from state offices of vital records for all probable matches, using a previously validated algorithm that included name, date of birth, sex, race, marital status, and state.[22] Three physicians independently verified the determination of each death. Two physicians categorized the cause of each death as due to cardiovascular disease or non-cardiovascular disease. Disagreements among raters were resolved by discussion. All-cause mortality was the primary outcome in all analyses, with cardiovascular and non-cardiovascular mortality as secondary outcomes.

Statistical Analysis

We used Cox proportional-hazards models to examine the relationship of marijuana use to mortality following adjustment. We first adjusted for age, sex, and their interaction.[23] In subsequent models, we further controlled for race, body-mass index (as linear and quadratic terms), marital status (married versus other), current smoking, previous smoking, usual frequency of exertion (in three categories), intake of tea (in three categories), usual intake of alcohol (in three categories), binge drinking, household income (in quartiles), educational attainment (in three categories), previous AMI, previous congestive heart failure, diabetes mellitus, hypertension, non-cardiac comorbidity, previous medication use (aspirin, β-adrenergic antagonists, calcium-channel blockers, digoxin, diuretics, hypolipidemic agents, and angiotensin-converting-enzyme inhibitors individually), and receipt of thrombolytic therapy. We assigned indicator variables for patients with missing information on educational attainment (n=58), household income (n=60), tea intake (n=33), and smoking (n=20) and set body-mass index to the mean for 21 patients with missing information. Models that excluded individuals with any missing covariate information yielded similar results and are not shown here.

As a sensitivity analysis, we matched marijuana users with an equal number of other patients using propensity scores.[24] Each patient's score is that individual's probability that he or she would report marijuana use, based upon demographic, behavioral, and clinical characteristics. To create propensity scores, we used a multivariable logistic regression model, in which the dependent variable was marijuana use, and the independent variables were all covariates used in the Cox models noted above except receipt of thrombolytic therapy, and with the addition of linear and quadratic terms for age and alcohol use and interaction terms of sex with age and race. The area under the receiver operating characteristics (ROC) curve was 0.96, indicating outstanding discrimination for the logistic model. We then individually matched marijuana users to unique non-users using the nearest available pair matching method.[25] We were successfully able to match 42 marijuana users to 42 unique patients who did not report such use; the remainder had disjoint ranges of propensity scores. We compared Kaplan-Meier estimates of survival among these 84 patients using the log-rank test.

We tested the proportionality of hazards using time-varying covariates and found no significant violations. We used the SAS System for Windows, release 8.01 (SAS Institute, Inc., Cary, NC)

for all analyses. The funding sources for this work had no role in the analysis, presentation, or publication of results.

Results

Patient Characteristics

Table 1 shows the characteristics of the Onset Study participants according to marijuana use. A total of 52 patients (2.7%) reported marijuana use in the preceding year. As expected,[5] marijuana users tended to be younger than other patients, had heavier usual alcohol consumption, and were more likely to be male, current smokers, and divorced or separated. Among marijuana users, the reported median frequency of use was once every two weeks.

Marijuana Use and Mortality

A total of 317 patients died during a median of 3.8 years of follow-up. Table 2 shows hazard ratios for mortality, comparing marijuana users to other participants. Marijuana use was associated with three-fold higher total mortality, both in age- and sex-adjusted and in more fully adjusted models.

To determine whether marijuana use was associated with a gradient in risk of death, we separated marijuana users into those reporting use less than weekly versus weekly or more. Compared with non-users, use less than weekly was associated with a hazard ratio of 2.5 (95% confidence interval, 0.9−7.3). The corresponding hazard ratio for marijuana use weekly or more was 4.2 (95% confidence interval, 1.2−14.3).

Although we did not have sufficient numbers of cases to evaluate cardiovascular and non-cardiovascular mortality with precision, 4 of 7 deaths among marijuana users were non-cardiovascular, compared with 75 of 310 among non-users (p exact 0.07). The age- and sex-adjusted hazard ratios associated with any marijuana use were 1.9 (95% confidence interval, 0.6−6.3) for cardiovascular mortality and 4.9 (95% confidence interval, 1.6−14.7) for non-cardiovascular mortality.

Given that approximately three-quarters of marijuana smokers were also cigarette smokers, we repeated our analyses restricted to current smokers (who accounted for 62 deaths). The age- and sex-adjusted hazard ratio associated with marijuana use was 4.1 (95% confidence interval, 1.6−10.4). The corresponding hazard ratio when restricted to current consumers of alcohol was 3.7 (95% confidence interval, 1.5−9.1).

We also performed additional analyses in an attempt to ensure our models were robust. The hazard ratio associated with marijuana use was 2.9 (95% confidence interval, 1.2−6.7) when we controlled for concurrent use of cocaine, and 2.8 (95% confidence interval, 1.2−6.5) when we additionally controlled for initial hypotension, complications of congestive heart failure or ventricular arrhythymias during hospitalization, and peak creatine kinase levels as measures of infarct severity. The hazard ratio from a stepwise model (with entry and stay criteria of p=0.20) was 3.1 (95% confidence interval, 1.4−7.0). Additional adjustment for coffee intake and intensity of current smoking (in four categories) also did not alter our results (hazard ratio 3.1; 95% confidence interval, 1.3−7.5).

Matched-Pair Analysis

We also determined the survival of 42 marijuana users and 42 other patients matched on propensity score (which is the probability of reporting marijuana use given other baseline characteristics). These groups were generally well matched, including similar mean ages (44.1 years in both groups) and proportions of white participants (69% versus 71%) and current

smokers (71% versus 74%). Clinical characteristics of the index infarction, though not part of the matching algorithm, were also comparable, with identical proportions sustaining Q-wave infarctions (60%) and congestive heart failure (7%) and similar peak creatine kinase levels (2035 versus 1979 IU/L). Among these 84 matched patients, 6 marijuana users died, compared with only 1 non-user (log-rank p = 0.06).

Causes of Death among Marijuana Users

We performed a post-hoc examination of the death certificates of the seven patients who reported marijuana use and who died during follow-up. Of the three patients who died of cardiovascular causes, two died of progressive coronary heart disease and one from sudden cardiac death related to ventricular fibrillation. Of the four who died of non-cardiovascular causes, one died in a motor vehicle accident, one from acquired immunodeficiency syndrome (AIDS), one from carcinoma of the lung, and one from both lung cancer and AIDS.

Discussion

In this preliminary prospective cohort study of early survivors of acute myocardial infarction, marijuana use, as measured at the time of hospitalization, was associated with three-fold higher mortality following infarction. There was a gradient in risk, with the highest risk of death among individuals who used marijuana most frequently, and the risk was entirely unchanged by multivariate adjustment.

Marijuana use has important cardiovascular effects that could pose risk for patients with coronary heart disease. Among the best-defined of these is an increase in resting heart rate that can be selectively blocked by pretreatment with a cannabinoid receptor antagonist.[26] This effect may be related to the prolonged catecholamine release that marijuana can induce.[27] Marijuana use can also increase supine blood pressure, although it leads to orthostatic hypotension, postural dizziness, and even syncope in some cases.[28, 29]

At the same time that marijuana increases heart rate and, therefore, myocardial oxygen demand, it may also limit oxygen uptake. Marijuana smoking leads to a dose-dependent increase in carbon monoxide exposure[30] and even higher blood levels of carboxyhemoglobin than does cigarette smoking.[12] These effects have a demonstrably detrimental impact on patients with known coronary heart disease, in whom marijuana use decreases exercise time to the onset of angina by 50%, twice as great an effect as use of a standard cigarette.[31]

Marijuana use could also lead to higher risk of death among patients by interfering with adherence to standard therapies. Although the relationship of marijuana use and adherence to therapy among patients with coronary heart disease has not been evaluated, it may interfere with adherence to other life-saving medication, such as antiretroviral therapy for human immunodeficiency virus infection.[32] The effects of marijuana use on cognitive function could conceivably exacerbate this further.[33]

Over half of deaths among Onset Study participants who reported marijuana use were non-cardiovascular, a substantially higher proportion than in non-users. Despite the lack of specificity inherent in use of death certificates to assign accurate causes of death,[34] our results suggest that patients with coronary heart disease who use marijuana may be at particular for risk for all causes of death, and not recurrent cardiovascular disease alone. In this regard, the possible effects of marijuana use on unintentional injury and upper airway malignancy may be particularly important.[35, 36] Marijuana use also directly increases risk-taking behavior in some settings,[37, 38] but our findings were not altered by adjustment for other markers of risky behavior that were available, including binge drinking and cocaine use, perhaps because marijuana use was less strongly related to risk-taking in this relatively older aged cohort.

Similar to our findings, Sidney and colleagues also found that marijuana use was associated with AIDS-related death in men.[2] It seems likely that this, at least in part, reflects confounding by indication, in which marijuana is used for nausea or appetite stimulation. However, cannabinoids may also have direct immunosuppressive effects that could accelerate disease progression among susceptible individuals.[14] Further studies to understand the degree to which marijuana use could influence post-infarct mortality via direct cardiovascular effects, cognitive changes that reduce adherence, non-cardiovascular effects of marijuana, or simply other confounding factors related to marijuana use are clearly needed.

The Onset Study has both strengths and limitations. An important and perhaps unique strength is its assessment of marijuana use in a population of early survivors of myocardial infarction; to our knowledge, no comparable cohort studies exist. All participants were interviewed in a standardized manner during hospitalization for enzymatically confirmed infarcts, and a relatively large body of information on clinical and sociodemographic variables was obtained.

On the other hand, these results should be viewed as hypothesis-generating only. The number of marijuana smokers was relatively small, follow-up was limited to approximately four years, and the confidence limits around our estimates – even when they exclude the null – were relatively wide. The cohort was assembled in the early 1990s, and the association of marijuana use with prognosis, while collected prospectively, was not a primary aim. Although further follow-up of this cohort is not possible, and could be of limited value without updated assessments of marijuana, our results do point to the urgent need for larger and longer studies of marijuana use in comparable populations.

As with any observational study, we cannot prove cause-and-effect relationships, although it is unclear how a randomized trial to test our findings could be performed. Our results were also consistently unchanged by adjustment for a wide variety of clinical characteristics, including alcohol intake and smoking. Nonetheless, there are apt to be unmeasured confounding clinical or lifestyle factors that may be responsible for our findings.

We asked participants to report their usual marijuana use over the year prior to the infarction that resulted in their hospitalization and did not have information on post-MI use, which is likely to have differed from that measured here. Assuming that some marijuana users cease use following hospitalization, we may have underestimated the true effect of post-infarction marijuana use on survival. On the other hand, by assessing marijuana exposure prior to infarction and prior to follow-up, we minimized the potential bias that could affect assessment of post-infarction marijuana use alone if sicker patients give up marijuana use more often than healthier patients following hospitalization. Future studies should also include repeated assessments of marijuana use to address this possibility.

In conclusion, marijuana use was associated with three-fold greater mortality following acute myocardial infarction in this exploratory study, with a graded increase in risk with more frequent use. Because marijuana use appears to be increasing among middle-aged and older adults, this finding may have growing importance in the future. Although marijuana use does not appear to be associated with mortality among the general population, our results suggest that it may carry particular risks for vulnerable populations with established cardiovascular disease.

Acknowledgements

This study was supported by grants R01HL41016 from the National Heart, Lung, and Blood Institute, Bethesda, MD, R21AA014900 from the National Institute on Alcohol Abuse and Alcoholism, Bethesda, MD, and 9630115N from the American Heart Association, Dallas, TX for the Determinants of Myocardial Infarction Onset Study.

Grant Support: 9630115N, American Heart Association, Dallas, TX; R21AA14900, National Institute on Alcohol Abuse and Alcoholism, Bethesda, MD; R01HL41016, National Heart, Lung, and Blood Institute, Bethesda, MD

References

1. Compton WM, Grant BF, Colliver JD, Glantz MD, Stinson FS. Prevalence of marijuana use disorders in the United States: 1991−1992 and 2001−2002. JAMA 2004;291(17):2114–21. [PubMed: 15126440]
2. Sidney S, Beck JE, Tekawa IS, Quesenberry CP, Friedman GD. Marijuana use and mortality. Am J Public Health 1997;87(4):585–90. [PubMed: 9146436]
3. Andreasson S, Allebeck P. Cannabis and mortality among young men: a longitudinal study of Swedish conscripts. Scand J Soc Med 1990;18(1):9–15. [PubMed: 2320981]
4. Sidney S. Cardiovascular consequences of marijuana use. J Clin Pharmacol 2002;42(11 Suppl):64S–70S. [PubMed: 12412838]
5. Mittleman MA, Lewis RA, Maclure M, Sherwood JB, Muller JE. Triggering myocardial infarction by marijuana. Circulation 2001;103(23):2805–9. [PubMed: 11401936]
6. Kotsalou I, Georgoulias P, Karydas I, Fourlis S, Sioka C, Zoumboulidis A, et al. A rare case of myocardial infarction and ischemia in a cannabis-addicted patient. Clin Nucl Med 2007;32(2):130–1. [PubMed: 17242569]
7. Tatli E, Yilmaztepe M, Altun G, Altun A. Cannabis-induced coronary artery thrombosis and acute anterior myocardial infarction in a young man. Int J Cardiol 2007;120(3):420–2. [PubMed: 17097170]
8. Caldicott DG, Holmes J, Roberts-Thomson KC, Mahar L. Keep off the grass: marijuana use and acute cardiovascular events. Eur J Emerg Med 2005;12(5):236–44. [PubMed: 16175062]
9. Lindsay AC, Foale RA, Warren O, Henry JA. Cannabis as a precipitant of cardiovascular emergencies. Int J Cardiol 2005;104(2):230–2. [PubMed: 16168820]
10. Collins JS, Higginson JD, Boyle DM, Webb SW. Myocardial infarction during marijuana smoking in a young female. Eur Heart J 1985;6(7):637–8. [PubMed: 3876212]
11. Steffens S, Veillard NR, Arnaud C, Pelli G, Burger F, Staub C, et al. Low dose oral cannabinoid therapy reduces progression of atherosclerosis in mice. Nature 2005;434(7034):782–6. [PubMed: 15815632]
12. Wu TC, Tashkin DP, Djahed B, Rose JE. Pulmonary hazards of smoking marijuana as compared with tobacco. N Engl J Med 1988;318(6):347–51. [PubMed: 3340105]
13. Harrison GP, Jr. Gruber AJ, Hudson JI, Huestis MA, Yurgelun-Todd D. Cognitive measures in long-term cannabis users. J Clin Pharmacol 2002;42(11 Suppl):41S–47S. [PubMed: 12412835]
14. Friedman H, Newton C, Klein TW. Microbial infections, immunomodulation, and drugs of abuse. Clin Microbiol Rev 2003;16(2):209–19. [PubMed: 12692094]
15. Braun BL, Hannan P, Wolfson M, Jones-Webb R, Sidney S. Occupational attainment, smoking, alcohol intake, and marijuana use: ethnic-gender differences in the CARDIA study. Addict Behav 2000;25(3):399–414. [PubMed: 10890293]
16. Mittleman MA, Maclure M, Tofler GH, Sherwood JB, Goldberg RJ, Muller JE. Triggering of acute myocardial infarction by heavy physical exertion. Protection against triggering by regular exertion. Determinants of Myocardial Infarction Onset Study Investigators. N Engl J Med 1993;329(23):1677–83. [PubMed: 8232456]
17. Mukamal KJ, Maclure M, Muller JE, Sherwood JB, Mittleman MA. Prior alcohol consumption and mortality following acute myocardial infarction. JAMA 2001;285(15):1965–70. [PubMed: 11308432]
18. Mukamal KJ, Maclure M, Muller JE, Sherwood JB, Mittleman MA. Tea consumption and mortality after acute myocardial infarction. Circulation 2002;105(21):2476–81. [PubMed: 12034652]
19. Mukamal KJ, Maclure M, Muller JE, Sherwood JB, Mittleman MA. Caffeinated coffee consumption and mortality after acute myocardial infarction. Am Heart J 2004;147(6):999–1004. [PubMed: 15199347]
20. Mittleman MA, Maclure M, Sherwood JB, Mulry RP, Tofler GH, Jacobs SC, et al. Triggering of acute myocardial infarction onset by episodes of anger. Determinants of Myocardial Infarction Onset Study Investigators. Circulation 1995;92(7):1720–5. [PubMed: 7671353]

21. Mukamal KJ, Maclure M, Muller JE, Mittleman MA. Binge drinking and mortality after acute myocardial infarction. Circulation 2005;112(25):3839–45. [PubMed: 16365208]
22. Stampfer MJ, Willett WC, Speizer FE, Dysert DC, Lipnick R, Rosner B, et al. Test of the National Death Index. Am J Epidemiol 1984;119(5):837–9. [PubMed: 6720679]
23. Mukamal KJ, Muller JE, Maclure M, Sherwood JB, Mittleman MA. Evaluation of sex-related differences in survival after hospitalization for acute myocardial infarction. Am J Cardiol 2001;88 (7):768–71. [PubMed: 11589845]
24. Joffe MM, Rosenbaum PR. Invited commentary: propensity scores. Am J Epidemiol 1999;150(4): 327–33. [PubMed: 10453808]
25. Parsons, LS. Reducing bias in a propensity score matched-pair sample using greedy matching techniques; Proceedings of the Twenty-Sixth Annual SAS Users Group International Conference; Cary, NC: SAS Institute, Inc.. 2001; 2001. p. 214-226.
26. Huestis MA, Gorelick DA, Heishman SJ, Preston KL, Nelson RA, Moolchan ET, et al. Blockade of effects of smoked marijuana by the CB1-selective cannabinoid receptor antagonist SR141716. Arch Gen Psychiatry 2001;58(4):322–8. [PubMed: 11296091]
27. Gash A, Karliner JS, Janowsky D, Lake CR. Effects of smoking marihuana on left ventricular performance and plasma norepinephrine: studies in normal men. Ann Intern Med 1978;89(4):448–52. [PubMed: 697222]
28. Mathew RJ, Wilson WH, Davis R. Postural syncope after marijuana: a transcranial Doppler study of the hemodynamics. Pharmacol Biochem Behav 2003;75(2):309–18. [PubMed: 12873621]
29. Mathew RJ, Wilson WH, Humphreys D, Lowe JV, Wiethe KE. Middle cerebral artery velocity during upright posture after marijuana smoking. Acta Psychiatr Scand 1992;86(2):173–8. [PubMed: 1529742]
30. Azorlosa JL, Greenwald MK, Stitzer ML. Marijuana smoking: effects of varying puff volume and breathhold duration. J Pharmacol Exp Ther 1995;272(2):560–9. [PubMed: 7853169]
31. Aronow WS, Cassidy J. Effect of smoking marihuana and of a high-nicotine cigarette on angina pectoris. Clin Pharmacol Ther 1975;17(5):549–54. [PubMed: 1126112]
32. Tucker JS, Burnam MA, Sherbourne CD, Kung FY, Gifford AL. Substance use and mental health correlates of nonadherence to antiretroviral medications in a sample of patients with human immunodeficiency virus infection. Am J Med 2003;114(7):573–80. [PubMed: 12753881]
33. Kalant H. Adverse effects of cannabis on health: an update of the literature since 1996. Prog Neuropsychopharmacol Biol Psychiatry 2004;28(5):849–63. [PubMed: 15363608]
34. Lloyd-Jones DM, Martin DO, Larson MG, Levy D. Accuracy of death certificates for coding coronary heart disease as the cause of death. Ann Intern Med 1998;129(12):1020–6. [PubMed: 9867756]
35. Gerberich SG, Sidney S, Braun BL, Tekawa IS, Tolan KK, Quesenberry CP. Marijuana use and injury events resulting in hospitalization. Ann Epidemiol 2003;13(4):230–7. [PubMed: 12684188]
36. Mao L, Oh Y. Does marijuana or crack cocaine cause cancer? J Natl Cancer Inst 1998;90(16):1182–4. [PubMed: 9719073]
37. Lane SD, Yechiam E, Busemeyer JR. Application of a computational decision model to examine acute drug effects on human risk taking. Exp Clin Psychopharmacol 2006;14(2):254–64. [PubMed: 16756429]
38. Lane SD, Cherek DR, Tcheremissine OV, Lieving LM, Pietras CJ. Acute marijuana effects on human risk taking. Neuropsychopharmacology 2005;30(4):800–9. [PubMed: 15775958]

Table 1

Characteristics of 1913 Onset Study participants according to self-reported marijuana use.

	Marijuana Use	
	Yes (N=52)	**No (N=1861)**
Age (years)	42.6 ±8.8	62.0 ±12.3
Female	3 (6)	587 (32)
White	36 (69)	1681 (90)
Body-Mass Index (kg/m^2)	27.8 ±5.3	27.3 ±5.2
Current Cigarette Smoker	40 (77)	596 (32)
Former Cigarette Smoker	9 (17)	781 (42)
Divorced/Separated	13 (25)	157 (9)
Hypertension	12 (23)	830 (45)
Diabetes	4 (8)	389 (21)
Previous Myocardial Infarction	11 (21)	525 (28)
Angina	5 (10)	478 (26)
Previous Congestive Heart Failure	1 (2)	81 (4)
Non-Cardiac Comorbidity	2 (4)	280 (15)
Regular Use of		
ACE-Inhibitors	2 (4)	220 (12)
Aspirin	20 (38)	626 (34)
β-Blockers	4 (8)	383 (21)
Calcium-Channel Blockers	8 (15)	458 (25)
Digoxin	1 (2)	142 (8)
Hypolipidemics	3 (6)	139 (7)
Diuretics	2 (4)	377 (20)
Thrombolytic Use	21 (40)	664 (36)
First Systolic Blood Pressure <90 mm	4 (8)	51 (3)
Complications of		
Congestive Heart Failure	3 (6)	276 (15)
Ventricular Tachycardia	11 (21)	227 (12)
Q-Wave Infarction	18 (62)	568 (56)
Education (years of schooling)	12.4 ±4.0	12.7 ±3.0
Income ($)[2,8]	32873 ±13576	38523 ±13086
Weekly Tea Intake (cups)	3.7 ±8.0	4.2 ±9.5
Weekly Coffee Intake (cups)	23.8 ±31.7	16.5 ±24.5
Weekly Alcohol Intake (servings)	15.0 ±25.4	4.0 ±11.1

Mean values with standard deviations are shown for continuous variables, numbers with percentages in parentheses for categorical variables.

Table 2

Hazard ratios and 95% confidence intervals for all-cause, cardiovascular, and non-cardiovascular mortality following acute myocardial infarction according to marijuana use among Onset Study participants.

	Marijuana Use		
	No	Yes	P-value
Number	1861	52	
Deaths	310	7	
Age- and sex-adjusted	1.0	3.0	0.006
	Ref	(1.4−6.7)	
Adjusted model[1]	1.0	3.0	0.009
	Ref	(1.3−7.0)	

[1]The adjusted model included age, sex, body-mass index, marital status, race, income, education, physical activity, current smoking, former smoking, tea intake, usual and binge alcohol intake, medical history (previous AMI, congestive heart failure, diabetes, hypertension, and non-cardiac comorbidity), receipt of thrombolytic therapy, and medication use (aspirin, beta-blockers, calcium-channel antagonists, ACE inhibitors, digoxin, diuretics, and hypolipidemic agents).