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ORIGINAL RESEARCH

Association of Cannabis Use Disorder With Hospitalizations for Pulmonary Embolism and Subsequent in-Hospital Mortality in Young Adults: A Contemporary Nationwide Analysis

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BACKGROUND: With the increase in popularity of cannabis and its use and the lack of large-scale data on cannabis use and venous thromboembolism and pulmonary embolism (PE), we used a nationally representative cohort of young adults (aged 18–44 years) to compare the odds of admissions and in-hospital mortality of PE with and without cannabis use disorder (CUD).

METHODS AND RESULTS: Identified patients with PE using the National Inpatient Sample (2018) were compared for baseline, comorbidities, and outcomes. Multivariable regression analysis, adjusted for covariates, was used to compare the odds of PE in young patients with CUD (CUD+) versus those without (CUD–) and those with prior venous thromboembolism. Propensity score–matched analysis (1:6) was also performed to assess in-hospital outcomes. A total of 61 965 (0.7%) of 8 438 858 young adult admissions in 2018 were PE related, of which 1705 (0.6%) had CUD+. On both unadjusted (odds ratio, 0.80 [95% CI, 0.71–0.90]; $P<0.001$) and adjusted regression analyses, the CUD+ cohort had a lower risk of PE admission. The CUD+ cohort had fewer routine discharges (58.3% versus 68.3%) and higher transfers to short-term (7.9% versus 4.8%) and nursing/intermediate care (12.6% versus 9.5%) ($P<0.001$). The PE-CUD+ cohort of in-hospital mortality did not differ from the CUD– cohort. Propensity score–matched (1:6) analysis revealed comparable mortality odds with higher median hospital stay and cost in the CUD+ cohort.

CONCLUSIONS: Young adults with CUD demonstrated lower odds of PE hospitalizations without any association with subsequent in-hospital mortality. The median hospital stay of the CUD+ cohort was longer, they were often transferred to other facilities, and they had a higher cost.

Key Words: cannabis/marijuana ■ mortality ■ outcomes ■ pulmonary embolism ■ venous thromboembolism

In recent years, the use of cannabis (marijuana) has gained more popularity across the United States.[1] Cannabis has the properties of an illicit drug, which could cause someone to use it more frequently than necessary, resulting in addiction. Earlier reports have suggested its potential impact on mental health and cardiovascular health outcomes.[2] A 2-sample Mendelian randomization study performed in 2022

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CLINICAL PERSPECTIVE

What Is New?

- Cannabis use disorder is associated with lower risk of pulmonary embolism hospitalizations.
- The cohort with cannabis use disorder had longer hospital stays, higher transfer rates, and increased cost burden.
- Cannabis use disorder did not predict pulmonary embolism hospitalizations in patients with venous thromboembolism.

What Are the Clinical Implications?

- Cannabis use disorder was not associated with in-hospital mortality in pulmonary embolism–related admissions.

examined the association between cannabis use disorder (CUD) and cardiovascular diseases.[3] The genetic liability of CUD was reported to be associated with a higher risk of atrial fibrillation, heart failure, pulmonary embolism (PE), and stroke.[3] The legalization of cannabis has drawn much attention over the past few years and has garnered much curiosity among young and older adults alike. It is estimated that 1 in 10 people who smoke marijuana will become addicted, and the risk depends on use.[4] There have been recent reports published on the overlapping patterns of medical and recreational marijuana. Patients who use cannabis for medical purposes are more likely to continue to use it for recreational purposes, potentially leading to an addiction.[5] According to the most recent National Survey on Substance Use and Health, 40.3 million people aged ≥12 years in the United States had experienced substance use disorders within a single year.[6]

Venous thromboembolism (VTE) is an underdiagnosed and often serious but preventable medical condition. In the United States, the incidence of VTE is estimated at 117 per 100 000.[7] Because of the prevalent occurrence of misdiagnosis or delayed detection until postmortem examination, it is conceivable that the true prevalence of these diseases exceeds the reported figures. Deep vein thrombosis and PE can happen to anyone and cause serious disabilities and sometimes fatalities. PE is the direct cause of 5% to 10% of hospital deaths.[8] PE is frequently encountered in elderly individuals, but it can also occur in young adults.[9] The presentation of PE in younger adults is typically subtle. Pregnancy and contraceptive use are routinely absent as PE risk factors. Therefore, a significantly higher level of clinical suspicion for PE is required to diagnose PE in the younger adult population. This is crucial because the mortality rate of this potentially fatal disease is low when treated with the proper medication.[10] The prevalence of PE increases with age, with a higher incidence in women than in men.[11]

A growing body of evidence has demonstrated abnormalities in blood coagulation in association with cannabinoid use, suggesting the involvement of the endogenous cannabinoid system in modulating blood coagulation.[12] Despite an increase in the number of adults using cannabis both recreationally and medicinally and the number of patients experiencing PE, little is known about the association between cannabis use and VTE. We focused our efforts on CUD in this study, considering recent Canadian and American survey reports of nearly 80% endorsement and overlapping patterns of medicinal and recreational cannabis use.[5] The main goal of this nationwide study was to evaluate the impact of CUD on the incidence of PE-related hospitalizations in young adults, aged 18 to 44 years. We also conducted exploratory analysis to assess risk of other comorbidities and mortality among CUD cohorts. There are still significant gaps in our understanding of the relationship between CUD and PE that have important implications for public health and clinical practice and that this study aims to address.

METHODS

The data that support the findings of this study are available from the corresponding author on reasonable request.

We used the National Inpatient Sample from the Healthcare Cost and Utilization Project for the year 2018 to conduct a retrospective cohort analysis. The National Inpatient Sample is the nation's largest all-payer inpatient database, providing national estimates of hospitalizations and representing admissions from >45 states. Because the National Inpatient Sample does not disclose patient-identifiable data, our study did not require Institutional Review Board approval or informed consent.

The *International Classification of Diseases, Tenth Revision, Clinical Modification* (*ICD-10-CM*), code was used to identify young individuals, aged 18 to 44 years, who presented to the hospital with acute PE as their primary or secondary diagnosis (I2601, I2602, I2609, I2690, I2692, I2693, I2694, and I2699). Patients were classified as CUD positive (+) or CUD negative (–) based on their CUD status using pertinent *ICD-10* codes, F12.1× and F12.2× (excluding F12.21 dependence in remission). The *ICD-10* code Z86.71× was used to identify patients with history of VTE (Figure). The primary outcome of interest was the prevalence and odds of PE-related hospitalizations in young CUD+ patients versus those without CUD. Patients with a history of VTE were also studied to assess the odds of PE in the CUD+ and CUD– cohorts.

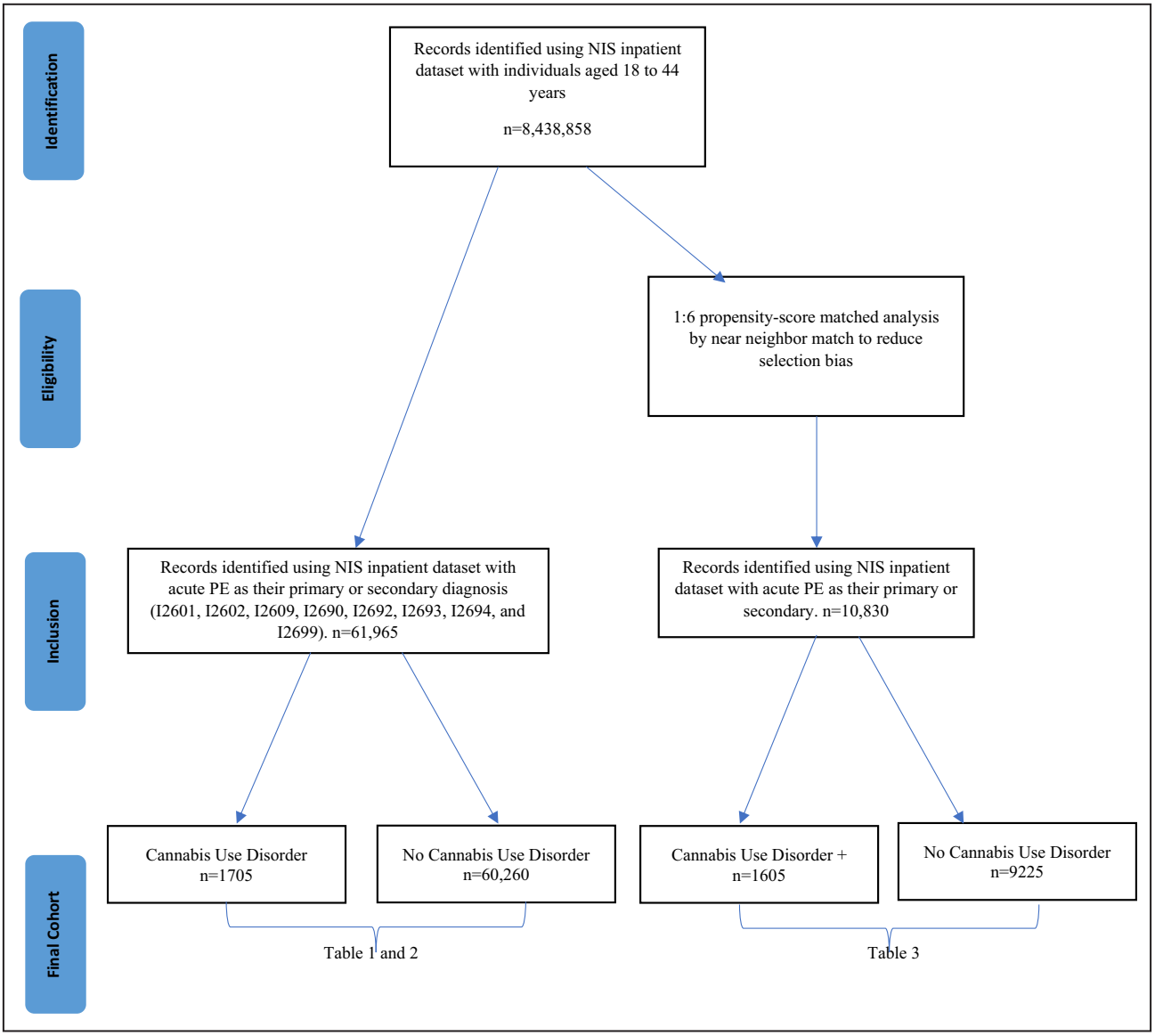

Figure 1. Decision flowchart of eligible records identified using the National Inpatient Sample (NIS) inpatient data set with acute pulmonary embolism (PE) and cannabis use disorder.

We used descriptive statistics to characterize and compare baseline characteristics of CUD+ and CUD– cohorts and outcomes. Frequencies and percentages were used to represent categorical variables. We used χ^2 tests to compare categorical data and Mann-Whitney *U* tests to compare continuous variables because of the nonnormal distribution of the data. To compare the odds of PE in young patients with CUD+ with those without CUD, a multivariable logistic regression analysis was performed. We also modified our model to account for potential confounding factors, such as age, sex, race or ethnicity, median household income, primary expected payer, comorbidities, like hypertension, diabetes, hyperlipidemia, congestive heart failure, valvular disease, pulmonary circulation disease, peripheral vascular disease, renal failure, liver disease, metastatic cancer, solid tumor with/without metastasis, rheumatoid arthritis, coagulopathy, obesity, prior myocardial infarction, prior stroke/transient ischemic attack, sepsis, deficiency anemias, smoking, drug abuse, psychoses, and depression, and hospital bed size/location or teaching status and regions. These variables were decided from prior or current literature. Similarly, we also evaluated the prevalence in patients who had a history of VTE as a different subgroup. To assess in-hospital outcomes in PE admissions while reducing selection bias, we conducted a 1:6 propensity score–matched analysis by near neighbor match to obtain CUD+ versus CUD– cohorts, with multivariable regression for age, sex, race, household income, and hospital region, with a caliper width of 0.01. All statistical testing was done with IBM SPSS Statistics,

Table 1. Baseline Characteristics and Comorbidities of Young Adults Hospitalized for Acute PE With Versus Without CUD

Characteristic	No CUD (n=60 260)	CUD (n=1705)	Overall acute PE admissions in young adults (aged 18–44 y) (n=61 965)	*P* value*
Age at admission, median (IQR), y				
	35 (29–40)	32 (27–37)	35 (29–40)	<0.001
Sex, %				
Male	43.3	56.9	43.6	<0.001
Female	56.7	43.1	56.4	
Race or ethnicity, %				
White	59.3	59.3	59.3	<0.001
Black	24.5	32.3	24.7	
Hispanic	10.9	7.2	10.8	
Asian or Pacific Islander/Native American/ others	5.3	1.2	5.2	
Median household income in the national quartile for patient zip code, %				
0–25th	33.8	44.2	34.1	<0.001
26th–50th	27.5	24.4	27.4	
51st–75th	22.8	21.3	22.7	
76th–100th	16.0	10.1	15.8	
Primary expected payer, %				
Medicare	8.7	7.6	8.7	<0.001
Medicaid	38.1	55.1	38.6	
Private, including HMO	37.4	16.1	36.9	
Self-pay	10.9	17.6	11.1	
No charges	1.2	1.8	1.2	
Others	3.5	1.8	3.5	
Location/teaching status of hospital, %				
Rural	5.6	5.9	5.6	0.018
Urban nonteaching	17.7	20.2	17.7	
Urban teaching	76.7	73.9	76.7	
Region of hospital, %				
Northeast	17.5	13.2	17.4	<0.001
Midwest	22.9	23.2	22.9	
South	41.7	44.0	41.8	
West	17.9	19.6	18.0	
Comorbidities, %				
Hypertension	25.4	24.0	25.4	0.206
Diabetes	11.3	9.4	11.2	0.014
Hyperlipidemia	7.7	5.6	7.7	0.001
Obesity	28.1	19.9	27.9	<0.001
Smoking	42.3	76.0	43.2	<0.001
Congestive heart failure	8.1	8.8	8.1	0.28
Valvular disease	7.8	15.5	8.0	<0.001
Pulmonary circulation disease	46.8	55.4	47.0	<0.001
Peripheral vascular disease	6.5	11.4	6.6	<0.001
Other neurologic disorders	6.4	9.4	6.4	<0.001
Prior MI	1.3	1.8	1.3	0.103
Prior TIA/stroke	1.9	3.5	1.9	<0.001
History of VTE	15.3	14.7	15.3	0.476

(*Continued*)

Table 1. Continued

Characteristic	No CUD (n=60 260)	CUD (n=1705)	Overall acute PE admissions in young adults (aged 18–44 y) (n=61 965)	*P* value*
Chronic pulmonary disease	15.0	17.6	15.1	0.003
Renal failure	5.6	5.9	5.6	0.577
Liver disease	7.9	11.4	8.0	<0.001
Metastatic cancer	3.2	2.1	3.1	0.01
Solid tumor without metastasis	1.5	0.9	1.5	0.032
Rheumatoid arthritis/collagen vascular diseases	3.5	2.9	3.5	0.189
Coagulopathy	12.5	16.4	12.6	<0.001
Sepsis	21.6	38.1	22.0	<0.001
Deficiency anemias	25.7	31.7	25.8	<0.001
Drug abuse	18.5	99.7	20.8	<0.001
Psychoses	6.7	12.9	6.9	<0.001
Depression	14.0	18.8	14.2	<0.001

CUD indicates cannabis use disorder; HMO, health maintenance organization; IQR, interquartile range; MI, myocardial infarction; PE, pulmonary embolism; TIA, transient ischemic attack; and VTE, venous thromboembolism.

*P<0.05 indicates statistical significance.

version 25.0 (IBM Corp, Armonk, NY) on weighted data with strata/cluster designs and complex survey modules, and results with P<0.05 were considered significant. We used the Strengthening the Reporting of Observational Studies in Epidemiology cohort checklist when writing our report.[13]

RESULTS

Results showed that of the 8 438 858 total young adult admissions in 2018, 61 965 (0.7%) were related to acute PE. On both the unadjusted (odds ratio [OR], 0.80 [95% CI, 0.71–0.90]; P<0.001) and adjusted (OR, 0.87 [95% CI, 0.78–0.96]; P=0.007) regression analyses, the odds of PE admission were lower in the CUD+ cohort compared with the CUD– cohort.

Patients in the CUD+ cohort were younger (median age, 32 versus 35 years) and more often men (56.9% versus 43.3%) compared with those in the CUD– group (P<0.001). Black race was more associated with the CUD+ cohort than others (32.3% versus 24.5%; P<0.001). Additionally, the CUD+ cohort had higher rates of smoking (76.0% versus 42.3%), valvular heart disease (15.5% versus 7.8%), chronic obstructive pulmonary disease (17.6% versus 15%), pulmonary circulation diseases (55.4% versus 46.8%), coagulopathy (16.4% versus 12.5%), sepsis (38.1% versus 21.6%), drug abuse (99.7% versus 18.5%), psychoses (12.9% versus 6.7%), depression (18.8% versus 14.0%), prior stroke (3.5% versus 1.9%), and liver disease (11.4% versus 7.9%), while having lower rates of diabetes (9.4% versus 6.4%), hyperlipidemia (5.6% versus 7.7%), obesity (19.9% versus 28.1%), and solid tumors without (0.9% versus 1.5%) and with metastatic cancer (2.1% versus 3.2%) (Table 1).

Both the univariate (3.2% versus 3.7%; P=0.366) and adjusted multivariable regression analyses (OR, 1.59 [95% CI, 0.82–3.09]; P=0.173) found no statistical difference of in-hospital mortality risk between the CUD+ cohort versus the CUD– cohort. The CUD+ cohort showed significantly lower home discharge (58.3% versus 68.3%) and a higher transfer to other facilities, like short-term facilities (7.9% versus 4.8%) and nursing/intermediate care institutions (12.6% versus 9.5%) compared with the CUD– cohort (P<0.001) (Table 2).

On the propensity-matched (1:6) analysis of the young inpatient PE cohort, comparing patients with CUD+ against those without CUD–, both groups presented with a median age of 32 years, with comparable sex and race distribution. A significant difference was identified in socioeconomic status, as evidenced by a higher proportion of CUD+ patients in the lowest income quartile. For comorbidities, the CUD+ group exhibited significantly higher rates of smoking, alcohol abuse, coagulopathy, along with a greater prevalence of prior transient ischemic attack/stroke, valvular disease, peripheral vascular disease, chronic pulmonary disease, and deficiency anemias, compared to with CUD– counterparts; however, the prevalence of hypertension and diabetes was comparable between cohorts.

Although the all-cause mortality rates were similar between the 2 groups (3.4% for CUD+ versus 3.9% for CUD–, with an adjusted OR of 0.96 [95% CI, 0.40–2.29]; P=0.928), CUD+ patients faced longer hospital stays (median, 6 versus 4 days) and higher health care costs (median USD, 12 758 versus 10 033) (Table 3).

Table 2. In-Hospital Outcomes and Multivariable Odds of PE-Related Hospitalizations and Subsequent In-Hospital Mortality in Young Patients With Versus Without CUD

Variable	No CUD (n=60 260)	CUD (n=1705)	Overall acute PE admissions in young adults (aged 18–44 y) (n=61 965)	*P* value*
Outcomes, %				
In-hospital mortality	3.7	3.2	3.6	0.366
Disposition of patient				
Routine	68.3	58.5	68.1	<0.001
Transfers to short term facility	4.8	7.9	4.9	
Other transfers, including SNF and ICF	9.5	12.6	9.6	
Home health care	8.2	4.1	8.1	
Length of stay, median (IQR), d				
	4 (2–9)	6 (3–13)	4 (2–9)	<0.001
Cost, median (IQR), USD				
	10 458 (5583–25 249)	13 192 (6328–27 155)	10 506 (5608–25 290)	<0.001

Association with PE-related admissions, adjusted for confounders					
Acute pulmonary embolism admissions		Adjusted odds ratio†	95% CI		*P* value
			Lower	Upper	
CUD	Yes vs no	0.87	0.78	0.96	0.007

Association with all-cause in-hospital mortality following PE admissions, adjusted for confounders					
In-hospital mortality		Adjusted odds ratio†	95% CI		*P* value
			Lower	Upper	
CUD	Yes vs no	1.59	0.82	3.09	0.173

CUD indicates cannabis use disorder; ICF, intermediate-care facility; PE, pulmonary embolism; IQR, interquartile range; and SNF, skilled nursing facility.

*$P<0.05$ indicates statistical significance.

†Multivariable regression analyses were adjusted for the following: age (years) at admission, sex, primary expected payer, race, median household income national quartile for patient zip code, elective vs nonelective admission, bed size, location/teaching status and region of hospital, comorbidities, including hypertension, diabetes, hyperlipidemia, smoking, obesity, peripheral vascular disease, congestive heart failure, valvular disease, prior myocardial infarction, prior transient ischemic attack/stroke, history of venous thromboembolism, personal history of cancer, pulmonary circulation disease, renal failure, liver disease, other neurologic disorders, chronic pulmonary disease, hypothyroidism, AIDS, lymphoma, metastatic cancer, solid tumor without metastasis, rheumatoid arthritis/collagen vascular diseases, coagulopathy, fluid and electrolyte disorders, chronic blood loss anemia, deficiency anemias, alcohol abuse, drug abuse, depression, and sepsis.

DISCUSSION

Substance use disorders are prevalent in North America, and CUD particularly is on the rise.[12] After the legalization of cannabis for medical and recreational use in some states, it is imperative to understand the potential impact on health, particularly PE.[14] PE is a significant cause of death worldwide,[15] and despite the high prevalence of cannabis use and PE, the correlation between the 2 remains unclear. Tetrahydrocannabinoids, which is a major psychoactive component of cannabis, can modulate the coagulation cascade and could result in hypercoagulability. However, the clinical relevance of these findings has never been investigated on a large scale.[16] To our knowledge, our study is the first step in looking into this potential relationship and analyzing the implications for public health and clinical practice to bridge the knowledge gaps, particularly focusing on young adults with CUD.

We discovered that individuals with CUD+ were less likely to experience PE than those without CUD. It is not clear that this finding is attributable to the direct effect of cannabis on the cardiovascular system, and causing vasodilation and low blood pressure could lower the risk of PE.[17] This finding is surprising given the known association between tetrahydrocannabinoids and platelet aggregation.[18] The study by Deusch et al showed that more research is needed to find out more about how tetrahydrocannabinoids affect blood clotting. The study showed that cannabinoid 1 and cannabinoid 2 were found on the cell membranes of human platelets, which may play a role.[18] On the contrary, it was also observed that the CUD+ group had a greater prevalence of comorbid conditions, such

Table 3. Postmatching (1:6) CUD+ Versus CUD– Cohorts Among Overall PE-Related Hospitalizations

Variable		No CUD (n=9225) (N, %)		CUD (n=1605) (N, %)		Overall PE-related hospitalizations (n=10 830) (N, %)		*P* value*
Age at admission, median (IQR), y		32 (27–38)		32 (27–37)		32 (27–38)		0.223
Sex								
Male		5210	56.5	920	57.3	6130	56.6	0.529
Female		4015	43.5	685	42.7	4700	43.4	
Race or ethnicity								
White		5560	60.3	945	58.9	6505	60.1	0.216
Black		2930	31.8	530	33.0	3460	31.9	
Hispanic		705	7.6	120	7.5	825	7.6	
Asian or Pacific Islander/Native American/ others		30	0.3		<11	40	0.4	
Median household income national quartile for patient zip code region of hospital								
0–25th		3565	38.6	710	44.2	4275	39.5	<0.001
26th–50th		2485	26.9	390	24.3	2875	26.5	
51st–75th		2305	25.0	340	21.2	2645	24.4	
76th–100th		870	9.4	165	10.3	1035	9.6	
Region of hospital								
Northeast		1265	13.7	205	12.8	1470	13.6	0.643
Midwest		2180	23.6	380	23.7	2560	23.6	
South		4010	43.5	720	44.9	4730	43.7	
West		1770	19.2	300	18.7	2070	19.1	
Comorbidities								
Diabetes		965	10.5	155	9.7	1120	10.3	0.329
Hyperlipidemia		725	7.9	95	5.9	820	7.6	0.007
Hypertension		2350	25.5	400	24.9	2750	25.4	0.639
Smoking		3985	43.2	1225	76.3	5210	48.1	<0.001
Alcohol abuse		385	4.2	205	12.8	590	5.4	<0.001
Prior MI		150	1.6	30	1.9	180	1.7	0.482
Prior TIA/stroke		175	1.9	60	3.7	235	2.2	<0.001
History of VTE		1525	16.5	220	13.7	1745	16.1	0.005
Valvular disease		815	8.8	235	14.6	1050	9.7	<0.001
Peripheral vascular disease		650	7.0	190	11.8	840	7.8	<0.001
Chronic pulmonary disease		1355	14.7	285	17.8	1640	15.1	0.002
Hypothyroidism		360	3.9	20	1.2	380	3.5	<0.001
Coagulopathy		1055	11.4	265	16.5	1320	12.2	<0.001
Obesity		2400	26.0	315	19.6	2715	25.1	<0.001
Deficiency anemias		2130	23.1	505	31.5	2635	24.3	<0.001
Depression		1145	12.4	295	18.4	1440	13.3	<0.001
In-hospital outcomes								
All-cause mortality		355	3.9	55	3.4	410	3.8	0.425
	Multivariable odds	Adjusted OR		95% CI				*P* value
		0.96		0.40–2.29				0.928
Disposition of patient	Routine	6270	68.0	940	58.7	7210	66.6	<0.001
	Transfers to short-term facility	450	4.9	130	8.1	580	5.4	
	Other transfers, including SNF and ICF	870	9.4	200	12.5	1070	9.9	
	Home health care	715	7.8	70	4.4	785	7.3	

(*Continued*)

Table 3. Continued

Variable	No CUD (n=9225) (N, %)	CUD (n=1605) (N, %)	Overall PE-related hospitalizations (n=10 830) (N, %)	*P* value*
Length of stay, median (IQR), d	4 (2–10)	6 (3–12)	4 (2–10)	<0.001
Cost, median (IQR), USD	10 033 (5495–24 209)	12 758 (6306–27 014)	10 303 (5612–24 391)	<0.001

The 1:6 propensity score matching was performed, adjusting for age, sex, race, median household income quartile, and hospital region to obtain CUD+ vs CUD– cohorts by multivariable regression analysis. Multivariable logistic regression was adjusted for these demographic factors: age at admission, sex, race, median household income national quartile for patient zip code, region of hospital, health care access and type (elective vs nonelective admission, primary expected payer, and location/teaching status of hospital), and medical history and comorbidities (diabetes, hyperlipidemia, smoking, prior MI, prior TIA/stroke, history of VTE, valvular disease, hypertension, obesity, peripheral vascular disease, chronic pulmonary disease, hypothyroidism, coagulopathy, deficiency anemias, alcohol abuse, concomitant drug abuse, and depression). CUD indicates cannabis use disorder; ICF, intermediate-care facility; IQR, interquartile range; MI, myocardial infarction; OR, odds ratio; PE, pulmonary embolism; SNF, skilled nursing facility; TIA, transient ischemic attack; and VTE, venous thromboembolism.

*P<0.05 considered statistically significant.

as valvular disease, chronic obstructive pulmonary disease, coagulopathy, sepsis, drug abuse, and psychoses. This indicates that the CUD+ group experienced an increased burden of disorders that have the potential to cause VTE. According to a study by Vakharia et al, patients with CUD have higher risks of VTE following surgical procedures like total knee arthroplasty.[19] A study on the endocannabinoid system suggested strong evidence for the crosstalk between the endocannabinoid system and the coagulation system.[16] A study by Latif and Garg indicated that since legalization, both medical and recreational cannabis use have spiked, and many cases of myocardial infarction have been linked to cannabis use, especially in young, healthy individuals.[17] The study also indicated that the interaction between the endocannabinoid system and the autonomic nervous system could be linked to cardiovascular adverse events.[17] A systematic review of mortality attributable to cannabis use found no overall increase in mortality attributable to cannabis use but noted that the prevalence of respiratory failure had increased.[20] This finding also shows that there is conflicting evidence because of the complex nature of the cannabis plant and the different chemicals present in it that have not been fully studied. To date, >545 substances have been found in the different parts of the cannabis plant.[21] The phytocannabinoids are the most common type of metabolite, and they have a huge range of structures and biological functions.[20] With the relaxation of governing rules and legalization, there is a need for large-scale clinical research into the therapeutic use of cannabis and its phytochemicals. There is a need for further investigation into CUD and its effect on other comorbidities and PE.

After propensity score–matched analysis for PE admissions, the all-cause mortality rates for the 2 groups of our study were comparable: 3.4% for CUD+ and 3.9% for CUD– (OR, 0.96 [95% CI, 0.40–2.29]; P=0.928). However, CUD+ patients had longer hospital stays and more expensive care. These findings suggest that, although all-cause mortality rates were comparable, patients with CUD experienced more resource-intensive hospitalizations compared with those without CUD. Further research is needed to explore the factors contributing to these differences in health care use and costs. Additionally, understanding the impact of CUD on health care outcomes can inform targeted interventions to improve patient care and reduce health care costs.

It is important to consider some limitations when interpreting our results. First, our retrospective and observational study designs limit establishing causality between CUD and PE. Second, our reliance on national inpatient samples, which are administrative data subject to coding errors and limited clinical, and posthospitalization follow-up information may impact our findings. Third, our study's inclusion of only hospitalized patients limits the generalizability of our results to the general population. Finally, we did not collect data on cannabis consumption duration, amount, mode, or form, which could influence PE risk. Although CUD was not associated with in-hospital mortality in young adults hospitalized with PE, long-term outcomes should be evaluated in future prospective studies.

It is likely that in the future, more states adopting legalization will continue the trend of increased recreational cannabis consumption overlapping with medical cannabis. It has become more important to study the impact of CUD on younger adults and analyze the correlation between respiratory disorders, like PE, using larger and more inclusive samples.

CONCLUSIONS

Our study found that the odds of PE admissions were lower in young adults with CUD compared with the CUD– cohort, without any significant association with subsequent in-hospital mortality. But the current literature showing hypercoagulability in the CUD+ cohort attributable to tetrahydrocannabinoids presents contrary evidence. This finding warrants further, broader

investigation to determine the relationship between CUD and PE. Given the ever-growing use of cannabis recreationally, the significant overlap between medicinal and recreational use, and the high prevalence of PE, understanding the potential impact of cannabis use on the cardiovascular and pulmonary systems is important for public health and clinical practice.

ARTICLE INFORMATION

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REFERENCES

1. Volkow ND, Compton WM, Weiss SR. Adverse health effects of marijuana use. *N Engl J Med*. 2014;371:878–879. doi: 10.1056/NEJMc1407928
2. Seffah KD, Mahendar K, Namballa N, Pachchipulusu VK, Paudel Y, Patel A, Najam B, Desai HN, Illango J, Hamid P. To weed or not to weed: a systematic review exploring the potential for cannabis use in cardiovascular disease. *Mental Health Pain Management Cureus*. 2023;15:e40606. doi: 10.7759/cureus.40606
3. Chen M, Lu YL, Chen XF, Wang Z, Ma L. Association of cannabis use disorder with cardiovascular diseases: a two-sample Mendelian randomization study. *Front Cardiovasc Med*. 2022;9:966707. doi: 10.3389/fcvm.2022.966707
4. Copeland J, Swift W. Cannabis use disorder: epidemiology and management. *Int Rev Psychiatry*. 2009;21:96–103. doi: 10.1080/09540260902782745
5. Turna J, Balodis I, Munn C, Van Ameringen M, Busse J, MacKillop J. Overlapping patterns of recreational and medical cannabis use in a large community sample of cannabis users. *Compr Psychiatry*. 2020;102:152188. doi: 10.1016/j.comppsych.2020.152188
6. Substance Abuse and Mental Health Services Administration. *Key Substance Use and Mental Health Indicators in the United States: Results From the 2020 National Survey on Drug Use and Health (HHS Publication No. PEP21-07-01-003, NSDUH Series H-56)*. Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration; 2021. https://www.samhsa.gov/data/
7. Silverstein MD, Heit JA, Mohr DN, Petterson TM, O'Fallon WM, Melton LJ III. Trends in the incidence of deep vein thrombosis and pulmonary embolism: a 25-year population-based study. *Arch Intern Med*. 1998;158:585–593. doi: 10.1001/archinte.158.6.585
8. Shiraev TP, Omari A, Rushworth RL. Trends in pulmonary embolism morbidity and mortality in Australia. *Thromb Res*. 2013;132:19–25. doi: 10.1016/j.thromres.2013.04.032
9. Kruger DJ, Kruger JS, Collins RL. Cannabis enthusiasts' knowledge of medical treatment effectiveness and increased risks from cannabis use. *Am J Health Promot*. 2020;34:436–439. doi: 10.1177/0890117119899218
10. Cerdá M, Mauro C, Hamilton A, Levy NS, Santaella-Tenorio J, Hasin D, Wall MM, Keyes KM, Martins SS. Association between recreational marijuana legalization in the United States and changes in marijuana use and cannabis use disorder from 2008 to 2016. *JAMA Psychiatry*. 2020;77:165–171. doi: 10.1001/jamapsychiatry.2019.3254
11. Hammond CJ, Chaney A, Hendrickson B, Sharma P. Cannabis use among U.S. adolescents in the era of marijuana legalization: a review of changing use patterns, comorbidity, and health correlates. *Int Rev Psychiatry*. 2020;32:221–234. doi: 10.1080/09540261.2020.1713056
12. Khayat W, Lehmann C. The endocannabinoid system: a potential therapeutic target for coagulopathies. *Metabolites*. 2022;12:541. doi: 10.3390/metabo12060541
13. Vandenbroucke JP, von Elm E, Altman DG, Gøtzsche PC, Mulrow CD, Pocock SJ, Poole C, Schlesselman JJ, Egger M; STROBE Initiative. Strengthening the reporting of observational studies in epidemiology (Strobe): explanation and elaboration. *PLoS Med*. 2007;4:e297. doi: 10.1371/journal.pmed.0040297
14. Martinez Licha CR, McCurdy CM, Maldonado SM, Lee LS. Current management of acute pulmonary embolism. *Ann Thorac Cardiovasc Surg*. 2020;26:65–71. doi: 10.5761/atcs.ra.19-00158
15. Bondarenko AI. Cannabinoids and cardiovascular system. In: Bukiya AN, ed *Recent Advances in Cannabinoid Physiology and Pathology*. Vol 1162. Springer International Publishing; 2019:63–87. doi: 10.1007/978-3-030-21737-2_5
16. Stupinski J, Bible L, Asmar S, Chehab M, Douglas M, Ditillo M, Gries L, Khurrum M, Joseph B. Impact of marijuana on venous thromboembolic events: cannabinoids cause clots in trauma patients. *J Trauma Acute Care Surg*. 2020;89:125–131. doi: 10.1097/TA.0000000000002667
17. Latif Z, Garg N. The impact of marijuana on the cardiovascular system: a review of the most common cardiovascular events associated with marijuana use. *J Clin Med*. 2020;9:1925. doi: 10.3390/jcm9061925
18. Deusch E, Kress HG, Kraft B, Kozek-Langenecker SA. The procoagulatory effects of delta-9-tetrahydrocannabinol in human platelets. *Anesth Analg*. 2004;99:1127–1130. doi: 10.1213/01.ANE.0000131505.03006.74
19. Vakharia RM, Sodhi N, Anis HK, Ehiorobo JO, Mont MA, Roche MW. Patients who have cannabis use disorder have higher rates of venous Thromboemboli, readmission rates, and costs following primary Total knee arthroplasty. *J Arthroplast*. 2020;35:997–1002. doi: 10.1016/j.arth.2019.11.035
20. Drummer OH, Gerostamoulos D, Woodford NW. Cannabis as a cause of death: a review. *Forensic Sci Int*. 2019;298:298–306. doi: 10.1016/j.forsciint.2019.03.007
21. Hourfane S, Mechqoq H, Bekkali AY, Rocha JM, El Aouad N. A comprehensive review on cannabis sativa ethnobotany, phytochemistry, molecular docking and biological activities. *Plan Theory*. 2023;12:1245. doi: 10.3390/plants12061245