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Cannabis use disorder and mortality among patients with colon cancer

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Introduction

Cannabis use has been increasing in prevalence due to evolving legal frameworks and growing social acceptance [1]. Though often seen as benign, its long-term effects—especially in vulnerable groups like cancer patients—raise concerns. Cannabis use disorder (CUD), marked by problematic use, is linked to psychiatric comorbidities, cognitive dysfunction, respiratory complications, and immune system dysregulation [2]. Given that cancer outcomes depend on both biological and behavioral factors, understanding whether CUD modifies survival outcomes is of substantial clinical importance.

Emerging evidence suggests that cannabis may exert immunosuppressive effects, particularly through the modulation of T-cell function, which plays a crucial role in cancer immunosurveillance [3]. The endocannabinoid system may also promote tumor progression, especially in gastrointestinal malignancies [4]. While cannabinoids have demonstrated some anti-neoplastic properties in preclinical studies, their effects in human cancer populations remain complex and poorly understood [5]. Behaviorally, CUD is associated with increased psychiatric burden, including depression and anxiety, which can negatively influence cancer treatment adherence and prognosis [6]. Patients with substance use disorders, including CUD, are at higher risk for delayed diagnoses, suboptimal medical engagement, and lower adherence to recommended oncologic treatments [7].

Given these biological and behavioral considerations, there is a pressing need to investigate whether CUD influences cancer survival. To address this gap, we examined the association between pre-existing CUD and survival among patients with primary colon cancer.

Methods

This study utilized the University of California Health Data Warehouse (UCHDW), a comprehensive EHR-based repository spanning six medical centers from 2012 to 2024. The UCHDW adheres to the OMOP Common Data Model, enabling standardized coding of diagnoses, procedures, and laboratory values.

Eligible patients had a confirmed diagnosis of primary colon cancer and documented drug use disorder screening prior to cancer diagnosis. Inclusion further required available data on cannabis use disorder (CUD), age, and gender. Where available, disease severity was captured via Tumor, Node, Metastasis (TNM) staging and carcinoembryonic antigen (CEA) levels, a biomarker associated with colon cancer progression [8].

Metastatic stage was available for 96 % of patients, while T and N stages were available for 53 % and 55 %, respectively. Missing T and N values were imputed using multiple imputation by chained equations (MICE) based on associations with age and CEA. A validated rules-based algorithm was then applied to generate a four-category overall cancer stage [9].

CUD was defined as a clinical diagnosis documented prior to cancer diagnosis to mitigate potential reverse causation. The primary outcome was five-year all-cause mortality.

Logistic regression was employed to estimate odds ratios (ORs) between CUD and mortality, adjusting for age, gender and disease severity. Cox proportional hazards models were used to compute hazard ratios (HRs) to assess time-dependent risk of mortality. Statistical analyses were conducted using R on a Databricks Spark platform.

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Results

There were 1088 patients in this study with both a diagnosis of primary colon cancer and a pre-existing drug use disorder screening (Appendix Table 1). Patients with a history of CUD (n = 34) had a substantially higher five-year mortality rate (55.88 %) compared to patients without CUD (5.05 %).

Unadjusted logistic regression analysis demonstrated that CUD prior to cancer diagnosis was associated with a significantly increased odds of five-year mortality (OR = 24.40, 95 % CI: 11.39–52.34, $p < 0.001$). After adjusting for key demographic and clinical factors, including age, gender, and the CEA biomarker for disease severity, the association remained statistically significant, albeit attenuated (OR = 10.52, 95 % CI: 5.76–19.22, $p < 0.001$). This was retained when the stage was used in place of CEA as a measure of disease severity (OR = 8.21, 95 % CI: 4.56–12.98, $p < 0.001$).

In unadjusted Cox proportional hazards modeling, patients with pre-existing CUD had a HR of 10.52 (95 % CI: 5.76–19.22, $p < 0.001$), indicating a dramatic increased risk of mortality over time. The HR remained elevated after adjusting for demographics and disease severity, with a significant increase with use of the CEA biomarker (HR = 6.39, 95 % CI: 2.85–14.31, $p < 0.001$; Table 1a) and a marginally significant association when use of the four-category staging system (HR = 5.98, 95 % CI: 0.83–42.93, $p = 0.075$; Table 1b).

Table 1
Among patients with primary colon cancer, statistical output from multivariable Cox proportional hazards models relaying association between time to death for patients with pre-existing cannabis use disorder, with post hoc adjustment for gender, year of birth, and disease severity as measured by **(A)** the biomarker carcinoembryonic antigen and **(B)** the conventional four-category staging system.

Covariate	Hazard Ratio (HR)	95 % CI (Lower)	95 % CI (Upper)	p-value
(A)				
Cannabis Use Disorder	6.385	2.858	14.317	< 0.001
Female	0.645	0.298	1.395	0.265
Age (years)	0.977	0.955	0.999	0.048
Carcinoembryonic Antigen	1.001	1.000	1.002	0.011
(B)				
Cannabis Use Disorder	5.981	0.833	42.933	0.075
Female	1.282	0.357	4.599	0.704
Age (years)	0.962	0.984	1.100	0.168
Cancer Stage	2.462	0.654	9.262	0.183

Discussion

The results of this study indicate that a history of cannabis use disorder prior to colon cancer diagnosis is independently associated with an increased risk of mortality, even after adjusting for demographic and clinical confounders. These results suggest that pre-existing CUD may have a negative prognostic impact on cancer outcomes, warranting further investigation into potential biological, behavioral, and healthcare-related mechanisms.

Findings on the relationship between cannabis and cancer outcomes remain mixed and may depend heavily on patterns of use. While some preclinical studies suggest anti-tumor effects of cannabinoids such as THC [10], others associate chronic or high-intensity cannabis exposure with tumor progression, particularly in gastrointestinal malignancies [4]. The endocannabinoid system is known to modulate inflammation and immune function, and cannabinoids may impair anti-tumor immunity by inhibiting T-cell proliferation, suppressing antigen presentation, and altering cytokine signaling [11].

CUD is frequently comorbid with depression, anxiety, and cognitive impairment, all of which can compromise adherence to cancer therapies [6] diminishing treatment efficacy and increasing mortality risk [12]. Socioeconomic disadvantage, stigma, and competing health concerns may further limit access to timely, high-quality oncologic care among patients with CUD [13]. Moreover, elevated healthcare utilization for non-cancer conditions [14] may shift focus away from cancer management, contributing to poorer outcomes.

Several limitations warrant consideration. CUD identification via EHRs may result in misclassification, as clinical diagnoses may not reflect standardized criteria and could conflate therapeutic use with use disorder. Such misclassification is likely non-differential, potentially biasing results toward the null. Although CUD was required to precede cancer diagnosis, this does not preclude the presence of subclinical disease at the time of assessment or the possibility that cannabis use patterns changed after diagnosis, raising the potential for reverse causality. Residual confounding remains likely, particularly due to unmeasured factors such as socioeconomic status, lifestyle behaviors, and co-occurring substance use. As an observational study, causal inference is limited.

Future research should explore underlying mechanisms through prospective and mechanistic studies. In particular, incorporating structured assessments of cannabis use severity—such as validated screening instruments—would improve measurement of exposure and enhance interpretability of biological associations.

CRediT authorship contribution statement

Raphael E. Cuomo: Writing – review & editing, Writing – original draft, Validation, Software, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

Ethics Approval

This study is exempt from human subject protection under IRB protocol 1604619-1 of the University of California Health System.

Patient Consent Statement

Not applicable.

Funding

None.

Conflicts of Interest

None.

Permission to Reproduce Material from Other Sources

Not applicable.

Clinical Trial Registration

Not applicable.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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None.

Appendix

Table 1
Demographic and clinical characteristics of patients with primary colon cancer (N = 1088) included in the analytic cohort.

Characteristic	Value
Total patients	1088
Patients with CUD, n (%)	34 (3.1 %)
Mean age at cancer diagnosis (SD*)	59.17 (10.7) years
Female, n (%)	487 (44.8 %)
Median time from CUD diag. to cancer diag. (IQR†)	135 (35–522) days (before cancer)
Median CEA value (IQR)	2.1 (1.4–3.5) ng/mL
Mortality within 5 years, n (%)	70 (6.4 %)
Mortality among CUD patients, n (%)	19 (55.9 %)
Mortality among non-CUD patients, n (%)	51 (5.1 %)

* SD = Standard Deviation.
† IQR = Interquartile Range.

Data Availability Statement

The data that support the findings of this study are derived from the University of California Health Data Warehouse (UCHDW), which consists of de-identified patient information. Due to the sensitive nature of the clinical data and the agreements under which they were obtained, the data cannot be made publicly available.

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