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Original Article

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Cannabis Use and Its Association With Thirty- and Ninety-Day Hospital Readmissions for Patients Admitted for an Inflammatory Bowel Disease Exacerbation

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Abstract

Background: Though viewed as a potentially safer palliative alternative to opioids, studies of cannabis use for inflammatory bowel disease (IBD) are limited. The impact of opioids on hospital readmissions for IBD has been extensively examined, but cannabis has not been similarly studied. Our goal was to examine the relationship between cannabis use and the risk of 30- and 90-day hospital readmissions.

Methods: We conducted a review of all adults admitted for an IBD exacerbation from January 1, 2016 to March 1, 2020 within the Northwell Health Care system. Patients with an IBD exacerbation were identified by primary or secondary ICD10 code (K50.xx or K51.xx) and administration of intravenous (IV) solumedrol and/or biologic therapy. Admission documents were reviewed for the terms "marijuana", "cannabis", "pot" and "CBD".

Results: A total of 1,021 patient admissions met inclusion criteria, of whom 484 (47.40%) had Crohn's disease (CD) and 542 (53.09%) were female. Pre-admission cannabis use was reported by 74 (7.25%) patients. Factors found to be associated with cannabis use included younger age, male gender, African American/Black race, current tobacco and former alcohol use, anxiety, and depression. Cannabis use was found to be associated with 30-day readmission among patients with ulcerative colitis (UC), but not among patients with CD, after respectively adjusting each final model by other factors (odds ratio (OR): 2.48, 95% confidence interval (CI): 1.06 - 5.79 and OR: 0.59, 95% CI: 0.22 - 1.62, respectively). Cannabis use was not found to be associated with 90-day readmission on univariable analysis (OR: 1.11, 95% CI: 0.65 - 1.87) nor in the final multivariable model after adjusting for other factors (OR: 1.19, 95% CI: 0.68 - 2.05).

Conclusion: Pre-admission cannabis use was found to be associated with 30-day readmission among patients with UC, but not with 30-day readmission for patients with CD nor with 90-day readmission, following an IBD exacerbation.

Keywords: Crohn's disease; Ulcerative colitis; Inflammatory bowel disease; Cannabis; Opioids

Introduction

Inflammatory bowel disease (IBD), consisting primarily of ulcerative colitis (UC) and Crohn's disease (CD), is a chronic inflammatory condition affecting more than 1.5 million people in the United States [1]. Disease severity and/or complications frequently require hospitalization. These hospitalizations and high rates of hospital readmission are major factors contributing to the high cost of IBD-related care, and significantly diminish quality of life (QOL) in this population [2, 3]. It is widely acknowledged that factors associated with an increased risk of hospital readmission among IBD patients need to be better understood and addressed.

Prior analyses of factors associated with IBD hospital readmissions have included disease severity, corticosteroid use, surgical procedures, psychiatric disorders including anxiety and depression, psychological stressors, chronic pain and opioid use [1, 4-12]. Opioid use in the setting of IBD has been extensively studied. In addition to higher rates of hospital readmission, opioids have been associated with an increased risk of infection and death among IBD patients, and their use is generally discouraged in this population [13-16].

Given ongoing concerns regarding the use of opioids, many IBD patients have turned to cannabis as a potentially safer palliative alternative to opioids for symptom management. Cannabis use appears to be common in the IBD population with rates estimated as high as 10-12%, even prior to the legalization of cannabis in many states for both recreational and/or medical use [17]. New York State has specifically identified IBD as a condition qualifying those suffering to obtain medicinal cannabis legally. While studies of cannabis have not

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shown it to improve the inflammation associated with IBD, it may be an effective palliative therapy for complaints such as pain, anorexia and diarrhea [17-19]. However, as has long been the concern with opioid use, there is a risk that cannabis may merely mask complaints as the disease progresses, and/or patients may be tempted to underutilize or discontinue use of their standard IBD medications. Given the increasing use of cannabis in IBD, analyses for potential complications need to be conducted, as has been the case with opioids. The aim of this study was to examine the relationship between cannabis use and the risk of 30- and 90-day hospital readmissions among patients with IBD exacerbation.

Materials and Methods

Study design

IRB approval was obtained for a retrospective review of all adult IBD patients over the age of 18 who were admitted through the emergency room (ER), and underwent hospitalization for an IBD exacerbation from January 1, 2016 to March 1, 2020 within the Northwell Health Care system. The beginning date corresponds to the availability of legalized cannabis for IBD medicinal purposes in New York State. Patients were identified by either a primary or secondary ICD10 code (K50.xx, K51.xx), corresponding to CD or UC. The sample was limited to patients with an IBD exacerbation defined by administration of intravenous (IV) solumedrol and/or biologic therapy during the index admission. For patients with multiple admissions during the study period, only the first recorded admission was regarded as the index hospitalization, limiting each patient analyzed to one index admission. Pregnant patients and those who underwent an IBD-related surgery during the index admission were excluded from analysis.

Variables of interest

Patient characteristics and exposures examined included age in years, gender, disease type (CD vs. UC), race (African American/Black, Asian, other/multiracial, White), tobacco use (current, former, never, unknown), and alcohol use (current, former, never, unknown), a diagnosis of anxiety or depression, Charlson comorbidity index (CCI) score, index admission length of stay (LOS) in days and hospital opioid use. To assess for cannabis use prior to hospitalization, a natural language search of admission documents was performed for the terms "marijuana", "cannabis", "pot" and "CBD". Manual chart review was then performed to confirm cannabis use. Cannabis use was categorized as either active, past or none. Active cannabis use was further classified as medicinal, recreational, or unknown.

Outcomes

The co-primary outcomes of interest were 30-day readmission and 90-day readmission inclusive of ER encounters. Analysis was limited to a single readmission event following the first/index admission for each patient.

Statistical analysis

Demographic and clinical characteristics were summarized descriptively overall and by outcome group for each aim (i.e., cannabis use, 30-day readmission, 90-day readmission). Specifically, categorical variables were summarized using frequencies and percentages, and continuous variables were summarized using means and standard deviations (SDs).

To assess the association between each main exposure and outcome of interest, a series of separate logistic regression models were used. First, the interaction between cannabis use and IBD type was assessed to determine whether the relationship between cannabis use and 30-day or 90-day readmission differed by IBD type. If interaction was identified, analyses were stratified by IBD type. A univariable screen with a cut-off of $P < 0.20$ was then applied to identify covariates that could potentially be associated with each outcome of interest. If a variable was found to meet the screening threshold or was one of the main characteristics/exposures of interest (i.e., cannabis use and hospital opioid use), it was then included in a preliminary multivariable model. Backwards elimination was then applied, and main characteristics of interest were added back in when dropped to reach a final multivariable model for each outcome.

All analyses were completed using R version 4.1.2, and a P-value < 0.05 was considered statistically significant unless otherwise noted. This study was conducted in compliance with the ethical standards of Northwell Health on human subjects as well as with the Helsinki declaration.

Results

A total of 1,021 patients were identified who were admitted for an IBD exacerbation within the study period, of whom 484 (47.40%) had CD, 542 (53.09%) were female, and the mean ± SD age was 45.28 ± 20.24 years old. Pre-admission cannabis use was reported by 74 (7.25%) patients (Table 1). Cannabis use was most commonly reported to be recreational (63.00%) (Fig. 1). In total, 322 patients (31.54%) had any use of opioids during admission. On adjusted analysis, younger age was found to be associated with cannabis use, as were male gender, African American race, current tobacco use, former alcohol use, anxiety, and depression (Table 2).

30-day readmission

A total of 184 (18.02%) patients were readmitted within 30 days, 92 of whom had CD and 92 had UC. Assessment of interaction between cannabis use and IBD type for 30-day readmission was found to be significant, indicating that the relationship between cannabis use and 30-day readmission was found to differ by IBD type ($P = 0.0223$). Analyses were therefore

Table 1. Demographic and Patient Characteristics (N = 1,021)

Age (years)	
Mean (SD)	45.28 (20.24)
Gender	
Female	542 (53.09)
Male	479 (46.91)
Race	
African American/Black	150 (14.69)
Asian	54 (5.29)
Other/multiracial	143 (14.01)
White	674 (66.01)
Cannabis use	
Yes	74 (7.25)
No	947 (92.75)
Hospital opioid use	
Yes	322 (31.54)
No	699 (68.46)
Tobacco use	
Current	100 (9.79)
Former	172 (16.85)
Never	617 (60.43)
Unknown	132 (12.93)
Alcohol use	
Current	179 (17.53)
Former	24 (2.35)
Never	408 (39.96)
Unknown	410 (40.16)
IBD type	
Crohn's disease	484 (47.40)
Ulcerative colitis	537 (52.60)
CCI	
Mean (SD)	2.17 (2.88)
LOS (days)	
Mean (SD)	6.39 (7.11)

CCI: Charlson comorbidity index; IBD: inflammatory bowel disease; LOS: length of stay; SD: standard deviation.

stratified by IBD type (CD and UC) (Tables 3 and 4, respectively).

For CD, variables selected using the univariable screen to be used in the preliminary multivariable model included cannabis use, hospital opioid use, race, history of depression, CCI, and LOS on index hospitalization. Cannabis use was not found to be associated with 30-day readmission on univariable analysis nor in the final multivariable analysis adjusting for hospital opioid use, race, depression, and CCI (odds ratio (OR): 0.55, 95% confidence interval (CI): 0.21 - 1.45 and OR: 0.59, 95% CI: 0.22 - 1.62, respectively). Hospital opioid use was also not found to be associated with 30-day readmission on univariable analysis nor in the final multivariable analysis adjusting for cannabis use, race, depression, and CCI (OR: 1.45, 95% CI: 0.91 - 2.31 and OR: 1.45, 95% CI: 0.89 - 2.33, respectively). The final multivariable model indicated that African American/Black race, other/multiracial race, and higher CCI were risk factors for 30-day readmissions.

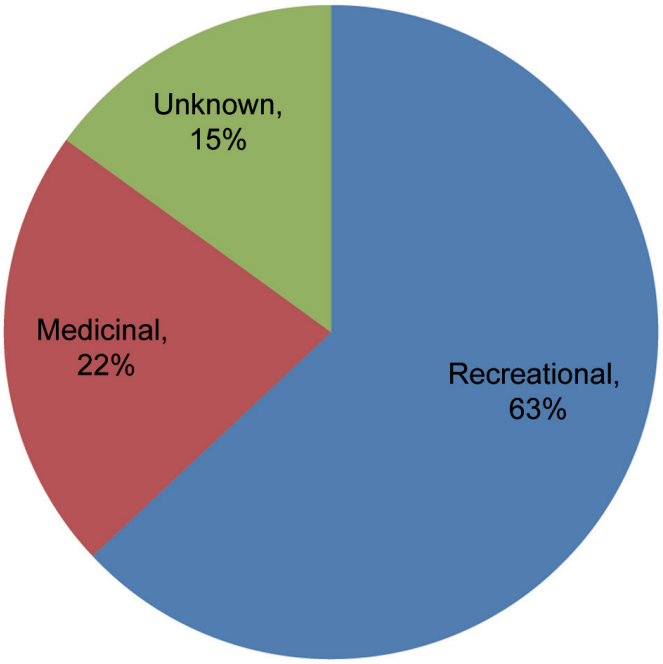

Figure 1. Cannabis use classifications.

For UC, variables selected using the univariable screen to be used in the preliminary multivariable model included cannabis use, hospital opioid use, age, race, tobacco use, alcohol use, CCI, and LOS on index hospitalization. Cannabis use was found to be associated with 30-day readmission on univariable analysis as well as in the final multivariable analysis after adjusting for hospital opioid use, race, and LOS on index hospitalization (OR: 2.35, 95% CI: 01.07 - 5.14 and OR: 2.48, 95% CI: 1.06 - 5.79, respectively). Hospital opioid use was again not found to be associated with 30-day readmission on univariable analysis nor in the final multivariable analysis adjusting for cannabis use, race, and LOS on index hospitalization (OR: 1.01, 95% CI: 0.61 - 1.66 and OR: 0.79, 95% CI: 0.46 - 1.36, respectively). The final multivariable model also indicated that African American/Black race, other/multiracial race, and longer LOS on index hospitalization were risk factors for 30-day readmissions.

90-day readmission

Assessment of interaction between cannabis use and IBD type for 90-day readmission was not found to be significant, indicating that the relationship between cannabis use and 90-day readmission was not found to differ by IBD type (P = 0.1249). A total of 271 patients (26.54%) were readmitted within 90

Table 2. Association Between Pre-Admission Characteristics and Cannabis Use (N = 1,021)

	Cannabis use (n = 74), n (%)	No cannabis use (n = 947), n (%)	Univariable OR (95% CI)	P-value	Multivariable OR (95% CI)	P-value
Patient characteristics						
Age (years)						
Mean (SD)	36.46 (15.52)	45.97 (20.41)	0.97 (0.96 - 0.99)	0.0001	0.96 (0.94 - 0.98)	< 0.0001
Gender						
Female	22 (29.73)	520 (54.91)	0.35 (0.21 - 0.58)	< 0.0001	0.28 (0.16 - 0.50)	< 0.0001
Male	52 (70.27)	427 (45.09)	Reference		Reference	
Race						
African American/Black	21 (28.38)	129 (13.62)	2.51 (1.44 - 4.40)	0.0012	2.80 (1.50 - 5.23)	0.0012
Asian	3 (4.05)	51 (5.39)	0.90 (0.27 - 3.04)	0.8757	1.12 (0.31 - 3.96)	0.8667
Other/multiracial	9 (12.16)	134 (14.15)	1.04 (0.49 - 2.19)	0.9240	1.11 (0.50 - 2.48)	0.7978
White	41 (55.41)	633 (66.84)	Reference		Reference	
Tobacco use						
Current	17 (22.97)	83 (8.76)	3.32 (1.78 - 6.16)	0.0002	2.97 (1.48 - 6.02)	0.0022
Former	12 (16.22)	160 (16.90)	1.21 (0.61 - 2.38)	0.5800	1.70 (0.78 - 3.71)	0.1788
Never	36 (48.65)	581 (61.35)	Reference		Reference	
Unknown	9 (12.16)	123 (12.99)	1.19 (0.55 - 2.52)	0.6664	1.26 (0.50 - 3.16)	0.6319
Alcohol use						
Current	17 (22.97)	162 (17.11)	1.32 (0.71 - 2.47)	0.3794	1.04 (0.53 - 2.07)	0.8998
Former	6 (8.11)	18 (1.90)	4.22 (1.55 - 11.38)	0.0047	3.71 (1.20 - 11.36)	0.0227
Never	30 (40.54)	378 (39.92)	Reference		Reference	
Unknown	21 (28.38)	389 (41.08)	0.68 (0.38 - 1.21)	0.1892	0.51 (0.25 - 1.04)	0.0644
Clinical characteristics						
Anxiety						
Yes	14 (18.92)	91 (9.61)	2.20 (1.18 - 4.09)	0.0130	2.72 (1.30 - 5.70)	0.0080
No	60 (81.08)	856 (90.39)	Reference		Reference	
Depression						
Yes	12 (16.22)	53 (5.60)	3.25 (1.66 - 6.43)	0.0006	3.97 (1.78 - 8.87)	0.0007
No	62 (83.78)	894 (94.40)	Reference		Reference	
IBD type						
Crohn's disease	42 (56.76)	442 (46.67)	1.51 (0.93 - 2.42)	0.0961	-	-
Ulcerative colitis	32 (43.24)	505 (53.33)	Reference		-	-
CCI						
Mean (SD)	1.35 (2.35)	2.23 (2.90)	0.87 (0.78 - 0.97)	0.0124	-	-

CCI: Charlson comorbidity index; CI: confidence interval; IBD: inflammatory bowel disease; OR: odds ratio; SD: standard deviation.

days (Table 5). Using the univariable screen, cannabis use, hospital opioid use, age, gender, tobacco use, alcohol use, IBD type, CCI, and LOS on index hospitalization were selected to be included in the preliminary multivariable model. On univariable analysis as well as in the final multivariable model after applying backwards elimination, neither cannabis use (OR: 1.11, 95% CI: 0.65 - 1.87 and OR: 1.19, 95% CI: 0.68 - 2.05, respectively), nor hospital opioid use (OR: 1.16, 95% CI: 0.86 - 1.56 and OR: 1.01, 95% CI: 0.74 - 1.37, respectively) were found to be associated with 90-day readmission. However, younger age, CD, higher CCI, and longer LOS on index hospitalization were found to be risk factors for 90-day readmission.

There were 15 patients found to have a readmission within 30 days, and 21 patients found to have a readmission within 90 days among patients with a history of cannabis use. For both 30-day and 90-day readmissions, the majority of patients were readmitted due to a non-IBD related ("other") cause, 11 (73.33%) and 12 (57.14%) respectively.

Table 3. Association Between Cannabis Use and Hospital Opioid Use With 30-Day Readmission Among Patients With Crohn's Disease (N = 484)

	Yes (n = 92), n (%)	No (n = 392), n (%)	Univariable OR (95% CI)	P-value	Multivariable OR (95% CI)	P-value
Main exposures						
Cannabis use						
Yes	5 (5.43)	37 (9.44)	0.55 (0.21 - 1.45)	0.2256	0.59 (0.22 - 1.62)	0.3079
No	87 (94.57)	355 (90.56)	Reference		Reference	
Hospital opioid use						
Yes	39 (42.39)	132 (33.67)	1.45 (0.91 - 2.31)	0.1166	1.45 (0.89 - 2.33)	0.1343
No	53 (57.61)	260 (66.33)	Reference		Reference	
Patient characteristics						
Age (years)						
Mean (SD)	44.64 (19.12)	44.34 (19.15)	1.00 (0.99 - 1.01)	0.8924	-	-
Gender						
Female	48 (52.17)	212 (54.08)	0.92 (0.59 - 1.46)	0.7412	-	-
Male	44 (47.83)	180 (45.92)	Reference		-	-
Race						
African American/Black	21 (22.83)	64 (16.33)	1.68 (0.95 - 3.01)	0.0731	1.99 (1.08 - 3.67)	0.0261
Asian	4 (4.35)	13 (3.32)	1.58 (0.50 - 5.06)	0.4360	2.12 (0.65 - 6.93)	0.2116
Other/multiracial	14 (15.22)	42 (10.71)	1.72 (0.87 - 3.37)	0.1152	2.01 (1.00 - 4.04)	0.0484
White	53 (57.61)	273 (69.64)	Reference			
Tobacco use						
Current	12 (13.04)	47 (11.99)	1.14 (0.57 - 2.30)	0.7144	-	-
Former	17 (18.48)	53 (13.52)	1.43 (0.77 - 2.67)	0.2575	-	-
Never	54 (58.70)	241 (61.48)	Reference		-	-
Unknown	9 (9.78)	51 (13.01)	0.79 (0.36 - 1.70)	0.5421	-	-
Alcohol use						
Current	13 (14.13)	71 (18.11)	0.76 (0.38 - 1.53)	0.4486	-	-
Former[a]	0 (0.00)	6 (1.53)	NA	NA	-	-
Never	38 (41.30)	159 (40.56)	Reference		-	-
Unknown	41 (44.57)	156 (39.80)	1.11 (0.67 - 1.80)	0.7059	-	-
Clinical characteristics						
Anxiety						
Yes	11 (11.96)	47 (11.99)	1.00 (0.49 - 2.01)	0.9929	-	-
No	81 (88.04)	345 (88.01)	Reference		-	-
Depression						
Yes	3 (3.26)	33 (8.42)	0.37 (0.11 - 1.23)	0.1024	0.35 (0.10 - 1.22)	0.0995
No	89 (96.74)	359 (91.58)	Reference			
CCI						
Mean (SD)	2.79 (3.59)	1.86 (2.40)	1.12 (1.11 - 1.23)	0.1024	1.15 (1.07 - 1.25)	0.0005
LOS (days)						
Mean (SD)	7.28 (6.33)	5.62 (7.70)	1.02 (1.00 - 1.05)	0.0790	-	-

[a]Odds ratio was not computed for former alcohol users due to low cell counts. CCI: Charlson comorbidity index; CI: confidence interval; LOS: length of stay; OR: odds ratio; SD: standard deviation.

Table 4. Association Between Cannabis Use and Hospital Opioid Use With 30-Day Readmission Among Patients With Ulcerative Colitis (N = 537)

	Yes (n = 92), n (%)	No (n = 445), n (%)	Univariable OR (95% CI)	P-value	Multivariable OR (95% CI)	P-value
Main exposures						
Cannabis use						
Yes	10 (10.87)	22 (4.94)	2.34 (1.07 - 5.14)	0.0331	2.48 (1.06 - 5.79)	0.0363
No	82 (89.13)	423 (95.06)	Reference		Reference	
Hospital opioid use						
Yes	26 (28.26)	125 (28.09)	1.01 (0.61 - 1.66)	0.9735	0.79 (0.46 - 1.36)	0.3958
No	66 (71.74)	320 (71.91)	Reference		Reference	
Patient characteristics						
Age (years)						
Mean (SD)	48.80 (22.15)	45.50 (20.97)	1.01 (1.00 - 1.02)	0.1740	-	-
Gender						
Female	49 (53.26)	233 (52.36)	1.04 (0.66 - 1.63)	0.8748	-	-
Male	43 (46.74)	212 (47.64)	Reference		-	-
Race						
African American/Black	7 (7.61)	58 (13.03)	0.47 (0.21 - 1.08)	0.0740	0.39 (0.16 - 0.95)	0.0369
Asian	5 (5.43)	32 (7.19)	0.61 (0.23 - 1.62)	0.3212	0.57 (0.21 - 1.55)	0.2698
Other/multiracial	9 (9.78)	78 (17.53)	0.45 (0.21 - 0.94)	0.0339	0.38 (0.18 - 0.84)	0.0163
White	71 (77.17)	277 (62.25)	Reference		Reference	
Tobacco use						
Current	5 (5.43)	36 (8.09)	0.77 (0.29 - 2.07)	0.6094	-	-
Former	23 (25.00)	79 (17.75)	1.62 (0.93 - 2.83)	0.0877	-	-
Never	49 (53.26)	273 (61.35)	Reference		-	-
Unknown	15 (16.30)	57 (12.81)	1.46 (0.77 - 2.80)	0.2449	-	-
Alcohol use						
Current	12 (13.04)	83 (18.65)	0.78 (0.38 - 1.59)	0.4926	-	-
Former	6 (6.52)	12 (2.70)	2.69 (0.94 - 7.71)	0.0635	-	-
Never	33 (35.87)	178 (40.00)	Reference		-	-
Unknown	41 (44.57)	172 (38.65)	1.28 (0.78 - 2.13)	0.3283	-	-
Clinical characteristics						
Anxiety						
Yes	7 (7.61)	40 (8.99)	0.84 (0.36 - 1.93)	0.6702	-	-
No	85 (92.39)	405 (91.01)	Reference		-	-
Depression						
Yes	5 (5.43)	24 (5.39)	1.01 (0.37 - 2.72)	0.9872	-	-
No	87 (94.57)	421 (94.61)	Reference		-	-
CCI						
Mean (SD)	2.99 (3.43)	2.14 (2.93)	1.08 (1.02 - 1.16)	0.0154	-	-
LOS (days)						
Mean (SD)	10.03 (9.77)	6.14 (5.71)	1.07 (1.04 - 1.10)	< 0.0001	1.07 (1.04 - 1.11)	< 0.0001

CCI: Charlson comorbidity index; CI: confidence interval; LOS: length of stay; OR: odds ratio; SD: standard deviation.

Table 5. Association Between Cannabis Use and Hospital Opioid Use With 90-Day Readmission (N = 1,021)

	Yes (n = 271), n (%)	No (n = 750), n (%)	Univariable OR (95% CI)	P-value	Multivariable OR (95% CI)	P-value
Main exposures						
Cannabis use						
Yes	21 (7.75)	53 (7.07)	1.11 (0.65 - 1.87)	0.7105	1.19 (0.68 - 2.05)	0.5537
No	250 (92.25)	697 (92.93)	Reference		Reference	
Hospital opioid use						
Yes	92 (33.95)	230 (30.67)	1.16 (0.86 - 1.56)	0.3192	1.01 (0.74 - 1.37)	0.9742
No	179 (66.05)	520 (69.33)	Reference		Reference	
Patient characteristics						
Age (years)						
Mean (SD)	46.79 (20.43)	44.73 (20.16)	1.01 (1.00 - 1.01)	0.1502	0.99 (0.98 - 1.00)	0.0127
Gender						
Female	118 (43.54)	361 (48.13)	1.21 (0.91 - 1.59)	0.1946	1.27 (0.95 - 1.70)	0.1024
Male	153 (56.46)	389 (51.87)	Reference		-	-
Race						
African American/Black	43 (15.87)	107 (14.27)	1.07 (0.72 - 1.58)	0.7347	-	-
Asian	12 (4.43)	42 (5.60)	0.76 (0.39 - 1.48)	0.4195	-	-
Other/multiracial	32 (11.81)	111 (14.80)	0.77 (0.50 - 1.18)	0.2263	-	-
White	184 (67.90)	490 (65.33)	Reference		-	-
Tobacco use						
Current	32 (11.81)	68 (9.07)	1.42 (0.89 - 2.24)	0.1376	-	-
Former	54 (19.93)	118 (15.73)	1.38 (0.95 - 1.99)	0.0910	-	-
Never	154 (56.83)	463 (61.73)	Reference		-	-
Unknown	31 (11.44)	101 (13.47)	0.92 (0.59 - 1.44)	0.7215	-	-
Alcohol use						
Current	38 (14.02)	141 (18.80)	0.70 (0.46 - 1.07)	0.0998	-	-
Former	7 (2.58)	17 (2.27)	1.07 (0.43 - 2.66)	0.8758	-	-
Never	113 (41.70)	295 (39.33)	Reference		-	-
Unknown	113 (41.70)	297 (39.60)	0.99 (0.73 - 1.35)	0.9655	-	-
Clinical characteristics						
Anxiety						
Yes	30 (11.07)	75 (10.00)	1.12 (0.72 - 1.75)	0.6193	-	-
No	241 (88.93)	675 (90.00)	Reference		-	-
Depression						
Yes	17 (6.27)	48 (6.40)	0.98 (0.55 - 1.73)	0.9415	-	-
No	254 (93.73)	702 (93.60)	Reference		-	-
IBD type						
Crohn's disease	141 (52.03)	343 (45.73)	1.28 (0.97 - 1.70)	0.0755	1.36 (1.02 - 1.81)	0.0363
Ulcerative colitis	130 (47.97)	407 (54.27)	Reference		Reference	
CCI						
Mean (SD)	2.80 (3.32)	1.94 (2.66)	1.11 (1.05 - 1.15)	< 0.0001	1.16 (1.08 - 1.25)	< 0.0001
LOS (days)						
Mean (SD)	8.10 (7.62)	5.77 (6.82)	1.04 (1.02 - 1.07)	< 0.0001	1.04 (1.02 - 1.06)	0.0002

CCI: Charlson comorbidity index; CI: confidence interval; IBD: inflammatory bowel disease; LOS: length of stay; OR: odds ratio; SD: standard deviation.

Discussion

Despite advances in care, IBD hospitalization and readmission continues to have a major impact both on the cost of care and QOL of IBD patients. Our observation of 18% readmission within 30 days and 26.5% within 90 days is in keeping with findings from other recent analyses from large academic centers, cohort studies and the National Readmissions Database (NRD). Our findings of more frequent readmission among patients with longer index hospitalizations and higher comorbidities have also been observed previously [4, 5, 10]. We observed significant associations between cannabis use and younger age, male gender, African American race, tobacco use, anxiety, depression and former alcohol use. We noted that former rather than current alcohol use was associated with cannabis. The study design would not allow for further analysis of this observation, though we speculate that cannabis may also serve as a "substitute" for those with prior alcohol use. For our primary outcomes, cannabis use was noted to be associated with 30-day, but not 90-day readmission in the UC cohort, and was not associated with either 30- or 90-day readmission for those with CD.

Notably, we did not find an association between opioid use during hospitalization and readmission. Prior analysis of this issue has been mixed. Charilaou et al's recent analysis of opioid use disorder (OUD) from the NRD from 2010 to 2014 observed a significant association with OUD and 30-day readmission, hazard ratio 1.47, 95% CI 1.28 - 1.69, $P < 0.001$ [20]. However, OUD, which was identified in only 1.4% of patients, appears to be a distinct entity from the far more common inpatient opioid use. We observed opioid use by almost a third of patients, also consistent with findings of other large cohort studies [21, 22] and recent meta-analysis [14]. A recent Cleveland Clinic cohort report from Hazratjee et al also found no association between inpatient opioid use and readmission, while noting that those discharged without opioids had a 2.2-fold increased risk for readmission [6].

Our study is among the first to examine cannabis use among patients hospitalized for IBD exacerbation. We found that slightly over 7% of patients reported pre-admission cannabis use, with a majority self-categorizing as recreational users. It is important to emphasize that various aspects of cannabis use vary across countries. Ransing et al demonstrated a higher prevalence of cannabis use among teenagers in countries such as South Africa, Italy and Spain [23]. Thailand in comparison demonstrated an overall decline in cannabis use across ages [23]. While the prevalence demonstrated in our study is lower than that of recent outpatient studies showing rates of active cannabis use of 10-12% [24, 25], it is similar to the findings of Dalal et al's recent cohort reporting 8% active cannabis use among IBD inpatients [21]. As was the case with descriptions of opioid use, the method of analysis of cannabis use appears to impact this figure. Micic et al's study of the NRD, utilizing the ICD code for cannabis dependence, reported a rate of only 1.6%. Cannabis dependence was associated with an increased risk of 30-day hospital readmission on univariate analysis, but not multivariate analysis [9]. Our analysis of cannabis use, as distinct from cannabis dependence, revealed an association between cannabis and 30-day readmission for patients with UC. In such a large registry as the NRD, it is impossible to say how precise the application of the diagnosis of cannabis dependence truly was, but the lower prevalence suggests a distinct and perhaps more medically significant entity from the more common cannabis use. Also, while our cohort showed similar rates of cannabis use to Dalal et al, we did not repeat their observation of higher inpatient opioid use by cannabis users, despite high rates of opioid use in each cohort. This leaves open the question of whether cannabis use is a "gateway" drug/predictor of future opioid use. Considering the increasing availability of cannabis, and the dismal history of opioids for IBD [26], this is an important question for future study.

Limitations to the study are those common to retrospective analysis of real-world data pulled from an electronic health record. While the methodology of the natural language search offered the ability to capture documentation of cannabis use beyond specific data point entries, it seems likely that many cannabis users were missed. Though documentation of cannabis use is encouraged by the electronic health record (EHR), it is not required to complete the admission process, at which time this history is typically recorded. Also, though cannabis use is becoming more accepted by society in general, it seems likely that the history of stigma and illegality associated with its use might cause some patients to withhold information of their own cannabis use. Also, while it would have been helpful for study purposes, urine toxicology for cannabis for objective evidence of use was (and is) not required at the study institutions, and was rare among those hospitalized for an IBD exacerbation. Though many of the typical cofactors associated with readmission were accessible by inpatient EHR data extraction, such as age, length of stay, and CCI, the data pull could not account for other factors that may have been associated with readmissions. Disease duration and severity quantified by accepted disease activity indices were not calculated during hospitalization for the study population and were therefore unknown. Also, post-discharge factors such as corticosteroid tapering and the timeliness of outpatient follow-up, which has also been observed to impact IBD readmissions [8], were not available for inclusion in our analysis. Also, we chose to include patients with a secondary admitting diagnosis of either CD or UC, but maintained the same standard of inpatient corticosteroid and/or biologic consistent with disease flare. This was intended to avoid excluding admissions for IBD for whom the admitting general medicine doctor may have preferred the use of an alternate primary admitting diagnostic code. Numbers of cannabidiol (CBD) users were also too few to perform any meaningful sub-analysis. Finally, the main limitation of the study was our inability to track cannabis use post discharge. Given the palliative properties of cannabis, it would be reasonable to assume that its use would continue or even increase following IBD hospitalization. This remains an assumption, leaving an unfilled gap in our knowledge of how cannabis use may impact rehospitalization.

In conclusion, our analysis of 30- and 90-day hospital readmissions in a large cohort of patients hospitalized with an IBD exacerbation confirmed risk factors for readmission including longer index hospitalization/LOS, and increased medical comorbidities. Inpatient opioid use was not associated with

hospital readmission. A history of cannabis use was not associated with more frequent readmissions following an CD exacerbation, but was for UC patients within 30 days. As cannabis use becomes more prevalent, and as its use as a palliative therapy becomes more accepted, further analyses will be needed to better understand its impact on long-term outcomes. The current study suggests a possible "red flag" in regards to cannabis use and rehospitalization, but further studies incorporating the outpatient IBD/cannabis experience post discharge are needed to further endorse its use in this important population.

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None to declare.

Conflict of Interest

The authors disclose no conflict of interest.

Informed Consent

Study obtained IRB approval to waive documented informed consent.

Author Contributions

Ellen Oseni: conception and design of the study; acquisition of data; drafting the article and revising it for critically important intellectual content. Miriam Blumenthal: acquisition of data; interpretation of data. Stephanie Izard: statistical analysis of data; interpretation of data; drafting the article and revising it for critically important intellectual content. Michael Qiu: acquisition of data. Anjali Mone: drafting the article and revising it for critically important intellectual content. Arun Swaminath: drafting the article and revising it for critically important intellectual content. Keith Sultan: conception and design of the study; interpretation of data; drafting the article and revising it for critically important intellectual content; final approval of the version to be submitted.

Data Availability

The data underlying this article cannot be shared publicly for the privacy of individuals that participated in the study. The data will be shared on reasonable request to the corresponding author.

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