

The Risk of Depression and All-Cause Mortality in Ulcerative Colitis Patients Maintained on Tofacitinib and Using Cannabis: A Population-Based Longitudinal Study

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Introduction

Background: Tofacitinib is used to treat moderate-to-severe ulcerative colitis (UC).

Aim: To investigate the risk of major depressive disorder (MDD) in patients with UC using tofacitinib.

Results

- Out of 205540 adult patients diagnosed with UC, 3095 (1.51%) used cannabis and 37265 (18.13%) used tobacco.
- 360 UC patients were maintained on tofacitinib between 2018-2021.
- Among cannabis users, the prevalence of MDD was 9.05% (71.32% females, 28.67% males).
- UC patients with MDD had increased all-cause mortality compared to those without MDD, 1.11% vs 0.01%.
- After adjusting for confounding in the multivariate analysis, cannabis use was an independent risk factor for MDD adjusted odds ratio (aOR) 3.87 (95%CI: 3.94-4.43, P< 0.001).

Major Depressive Disorder Risk Among UC Patients Using Tofacitinib and Cannabis

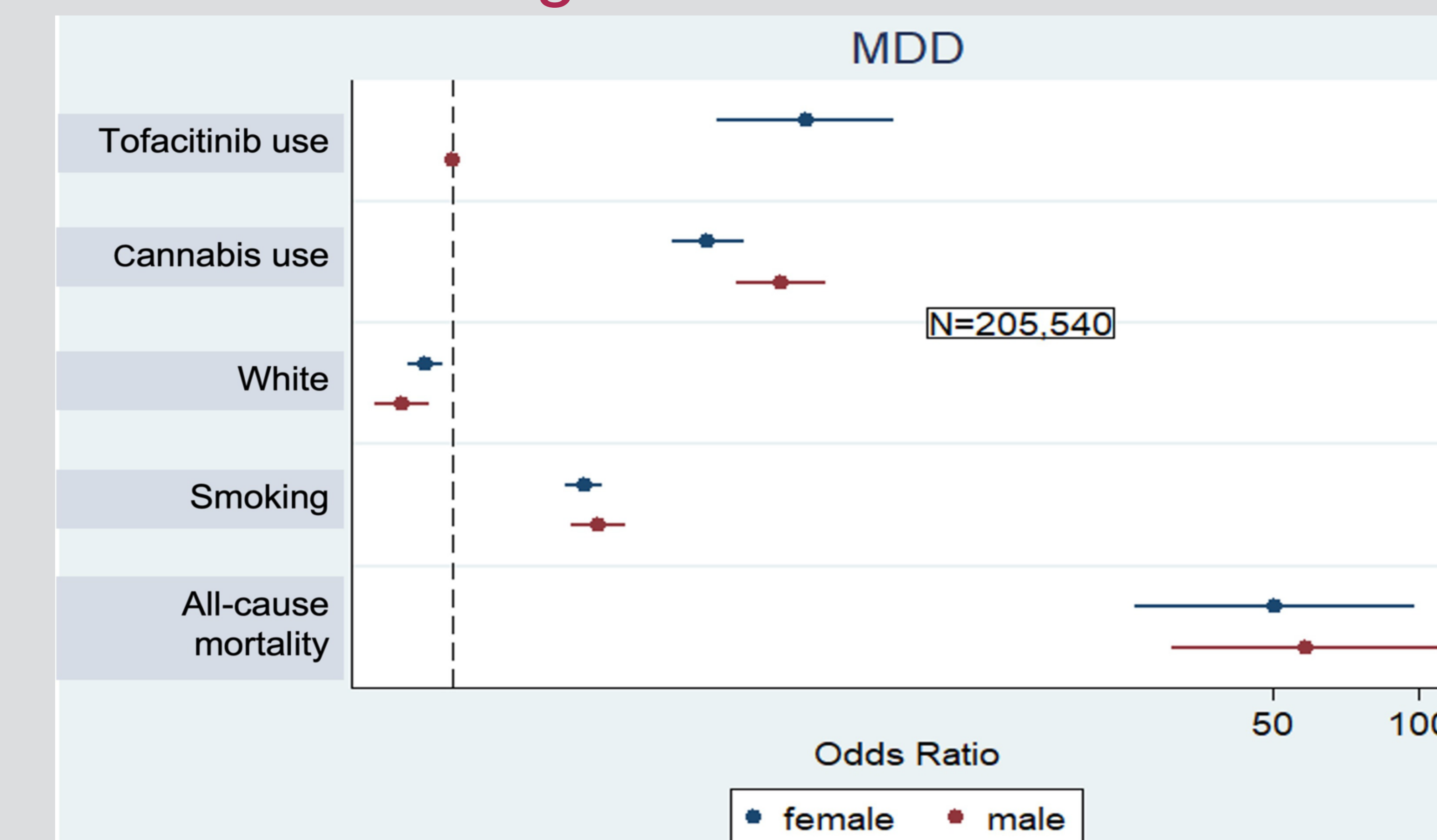


Figure. Multivariable logistic regression analysis of possible predictors for major depressive disorder (MDD) in patients with ulcerative colitis. Subgroup analysis stratified by gender. Forrest plot showing adjusted odds (OR); 95% confidence interval.

Methods

- Data was analyzed from a large database (Explorys, IBM) that provides electronic health records of patients from 26 major integrated US health care systems.
- Only adults with diagnosis of UC from January 1999-May 2021 were included.
- Among this cohort, race, gender, tofacitinib, cannabis, and tobacco use were examined.
- Primary and secondary outcomes were risk of MDD and all-cause mortality during December 2020-November 2021.
- Associations were estimated via gender-stratified multivariable logistic regression models.
- An interaction term was introduced to test the presence of effect modification.

Results

- UC patients using tofacitinib had higher odds of MDD diagnosis aOR 3.78 (95%CI: 2.51-5.71, P< 0.001).
- Smokers had higher risk of MDD compared to nonsmokers aOR 1.91 (95%CI: 1.77-2.04, P< 0.001). Whites had significantly lower risk of MDD compared to non-whites aOR 0.85 (95%CI: 0.79-0.91, P< 0.001).
- Males had significantly lower risk of MDD compared to females aOR 0.54 (95%CI: 0.50-0.58, P< 0.001).
- However, males risk of MDD significantly increased if they were also cannabis users aOR 1.48 (95%CI: 1.14-1.93; P< 0.001).
- Compared to males, females with UC had higher risk of MDD if they were using tofacitinib aOR 5.39 (95%CI: 3.54-8.21, P< 0.001).
- Overall, all-cause mortality was significantly higher in UC patients with MDD aOR 54.98 (95%CI, 34.55-87.49, P< 0.001).
- The odds of death increased by 0.5% above baseline in UC patients with MDD if they were prescribed tofacitinib.

Baseline characteristics of patients with ulcerative colitis included in the study						
Characteristics	MDD Diagnosis (N=1,495)			Absence of MDD Diagnosis (N=204,045)		
	Total (N)	Prevalence (%)	95% CI	Total (N)	Prevalence (%)	95% CI
Tofacitinib use						
Yes	25	0.62	0.41-0.91	335	0.16	0.14-0.18
No	4,020	99.38	99.08-99.58	201,160	99.84	99.81-99.85
Cannabis use						
Yes	280	6.92	6.17-7.74	2,815	1.39	1.34-1.44
No	3,765	93.07	92.25-93.82	198,680	98.61	98.55-98.65
Gender						
Male	1,160	28.68	27.30-30.09	84,560	41.97	41.75-42.18
Female	2,885	71.32	69.90-72.69	116,935	58.03	57.81-58.24
Race						
White	2,995	74.04	72.66-75.37	153,520	76.19	76.00-76.37
Non-White	1,050	25.96	24.62-27.33	47,975	23.81	23.62-23.99
Tobacco use						
Yes	1,270	31.39	29.98-32.84	35,995	17.86	17.69-18.03
No	2,775	68.6	67.15-70.01	165,500	82.13	81.96-82.31
All-cause mortality						
Yes	45	1.11	0.83-1.48	35	0.01	0.01-0.02
No	4,000	98.89	98.51-99.16	201,460	99.98	99.97-99.99

Table. Baseline characteristics of patients with ulcerative colitis included in the study. CI, confidence interval; MDD, major depressive disorder.

Conclusions

Cannabis use among UC patients is strongly associated with a diagnosis of MDD. UC patients (especially females) using tofacitinib have higher odds of being diagnosed with MDD. All-cause mortality is higher in UC patients if they are diagnosed with MDD.