



Short Report

Physician Practice Patterns in Holding Inflammatory Bowel Disease Medications due to COVID-19, in the SECURE-IBD Registry

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Abstract

Background: We aimed to describe physician practice patterns in holding or continuing IBD therapy in the setting of COVID-19 infection, using the Surveillance Epidemiology of Coronavirus Under Research Exclusion for Inflammatory Bowel Disease [SECURE-IBD] registry.

Methods: IBD medications that were stopped due to COVID-19 were recorded in the SECURE-IBD registry in addition to demographic and clinical data. We conducted descriptive analyses to understand characteristics associated with stopping IBD medications in response to active COVID-19 infection.

Results: Of 1499 patients, IBD medications were stopped in 518 [34.6%] patients. On bivariate and multivariable analyses, a diagnosis of ulcerative colitis or IBD-unspecified was associated with a lower odds of stopping medication compared with Crohn's disease (adjusted odds ratio [aOR] 0.6, 95% confidence interval [CI] 0.48, 0.75). When evaluating specific medications, 5-aminosalicylic acid was more likely to be continued [$p < 0.001$] whereas anti-tumour necrosis factor therapy and immunomodulator therapy were more likely to be stopped [global $p < 0.001$]. Other demographic and clinical characteristics did not affect prescription patterns.

Conclusions: IBD medications other than immunomodulators were continued in the majority of IBD patients with COVID-19, in the international SECURE-IBD registry. Future studies are needed to understand the impact of stopping or continuing IBD medications on IBD- and COVID-19 related outcomes.

Key Words: Inflammatory bowel disease; Crohn's disease; ulcerative colitis; coronavirus disease 2019; IBD therapy

1. Introduction

The impact of holding immunosuppressive and other therapies for inflammatory bowel diseases [IBD] in the context of coronavirus disease 2019 [COVID-19] is unknown. In the interim,

expert consensus is to hold corticosteroids, immunosuppressants, and biologics, but not 5-aminosalicylic acid [5-ASA], at the time of suspected or confirmed diagnosis of COVID-19 infection until fever and other symptoms are resolved.¹ There are currently no

Table 1. Demographic and clinical characteristics of IBD patients in the SECURE-IBD registry based on prescription practice in the setting of COVID-19.

Characteristic ^{a,b}	All patients on ≥1 medication		IBD medication stopped		IBD medication not stopped		p-value
	N [mean]	% [SD]	N [mean]	% [SD]	N [mean]	% [SD]	
Total number of patients	1499		518	31.8%	981	60.2%	-
Age	44	17.88	43	16.77	44	18.43	0.276
Female sex	752	48%	242	47%	485	49%	0.290
Race							
White	1221	81%	420	81%	801	82%	0.787
Black or African American	96	6%	35	7%	61	6%	0.685
American Indian/Native Alaskan	2	0%	1	0%	1	0%	0.646
Asian	87	6%	33	6%	54	6%	0.495
Native Hawaiian/Pacific Islander	0	0%	0	0%	0	0%	-
Other	115	8%	47	9%	68	7%	0.138
Hispanic/Latino							0.409
Yes	262	17%	100	19%	162	17%	
No	930	62%	314	61%	616	63%	
Unknown	186	12%	66	13%	120	12%	
Missing	121	8%	38	7%	83	8%	
Country							
USA	514	34%	172	33%	342	35%	0.520
Spain	225	15%	80	15%	145	15%	0.732
France	90	6%	32	6%	58	6%	0.837
Italy	74	5%	16	3%	58	6%	0.016
UK	71	5%	26	5%	45	5%	0.708
Iran	53	4%	20	4%	33	3%	0.620
Russian	79	5%	32	6%	47	5%	0.253
Brazil	50	3%	24	5%	26	3%	0.042
Other	343	23%	116	22%	227	23%	0.744
Disease type							<0.001
Crohn's disease	821	55%	325	63%	496	51%	
Ulcerative Colitis	649	43%	187	36%	462	47%	
IBD-unspecified	24	2%	4	1%	20	2%	
IBD disease activity ^c							0.702
Remission	854	57%	292	56%	562	57%	
Mild	273	18%	92	18%	181	18%	
Moderate	240	16%	90	17%	150	15%	
Severe	80	5%	24	5%	56	6%	
Comorbid conditions							
Any condition	555	37%	194	37%	361	37%	0.804
Cardiovascular disease	109	7%	32	6%	77	8%	0.236
Diabetes	88	6%	32	6%	56	6%	0.713
Lung disease	144	10%	42	8%	102	10%	0.153
Hypertension	194	13%	75	14%	119	12%	0.198
Cancer	33	2%	10	2%	23	2%	0.603
History of stroke	19	1%	5	1%	14	1%	0.447
Chronic renal disease	33	2%	8	2%	25	3%	0.208
Chronic liver disease	52	3%	17	3%	35	4%	0.774
Other	214	14%	77	15%	137	14%	0.636
Current smoker	63	4%	18	3%	45	5%	0.307
BMI							0.491
BMI <30	925	62%	315	61%	610	62%	
BMI ≥30	249	17%	82	16%	167	17%	
Missing	325	22%	121	23%	204	21%	
COVID-19 related emergency room visit	549	37%	188	36%	361	37%	0.847
COVID-19 related hospitalisation	422	28%	147	28%	275	28%	0.887

Statistically significant associations are in bold.

IBD, inflammatory bowel disease; SD, standard deviation; BMI, body mass index.

^aUnless otherwise specified, percentages do not include missing values or 'unknown'. For all characteristics, unless noted above, less than 4% of data were missing and unknown, respectively, for each category.

^bPercentages and *n* from each subcategory may not add up to the exact number of total reported cases, due to missing values and/or non-mutually exclusive variables.

^cBy physician global assessment [PGA] at time of COVID-19 infection.

Table 2. Multivariable analysis to determine factors associated with odds of stopping IBD medication in IBD patients with COVID-19.

Effect	Crude odds ratio	95% Wald confidence limits		<i>p</i> -value	Adjusted odds ratio	95% Wald confidence limits		<i>p</i> -value
Active vs remission	1.024	0.822	1.277	0.8296	0.971	0.772	1.221	0.8003
Unknown vs remission	1.203	0.676	2.14	0.5298	1.261	0.702	2.266	0.4375
UC/IBDU vs CD	0.607	0.489	0.755	<0.0001	0.597	0.478	0.747	<0.0001
USA vs non-USA	0.929	0.742	1.163	0.5203	0.943	0.704	1.264	0.6965
Spain vs non-Spain	1.053	0.783	1.417	0.7311	1.13	0.791	1.615	0.5015
France vs non-France	1.048	0.671	1.636	0.8361	1.029	0.63	1.68	0.9092
Italy vs non-Italy	0.507	0.289	0.892	0.0183	0.595	0.326	1.087	0.0916
UK vs non-UK	1.099	0.67	1.803	0.7081	1.154	0.674	1.975	0.6014
Iran vs non-Iran	1.154	0.655	2.032	0.6205	1.403	0.764	2.577	0.2748
Russia vs non-Russia	1.308	0.824	2.078	0.2544	1.477	0.882	2.472	0.1381
Brazil vs non-Brazil	1.785	1.014	3.141	0.0447	1.731	0.947	3.167	0.0748

Statistically significant associations are in bold.

UC, ulcerative colitis; IBD-U, IBD-unspecified; CD, Crohn's disease.

data on physician practice patterns regarding IBD therapy in the setting of COVID-19.

2. Methods

We analysed data from the Surveillance Epidemiology of Coronavirus Under Research Exclusion for Inflammatory Bowel Disease [SECURE-IBD] registry to determine physician practice patterns in IBD patients with confirmed COVID-19. Collection and categorisation of data have been previously reported.² Reporters to SECURE-IBD were asked if any medications were stopped due to active COVID-19 infection and to indicate which specific drugs were stopped.

We conducted bivariate analyses to understand demographic and clinical characteristics associated with stopping at least one IBD medication due to COVID-19, and subsequently performed multivariable logistic regression to evaluate the independent effects on IBD disease activity [specified a priori] and other patient characteristics that were statistically significant on bivariate analyses. We also analysed country as a variable affecting stopping in multivariate analyses and included any country with ≥ 50 reported cases in SECURE-IBD. Additionally, among users of each medication class, we compared the proportion of patients who had discontinued treatment after diagnosis of COVID-19; *p*-values ≤ 0.05 were considered statistically significant.

3. Results

Of 1499 patients with available medication-related data in the SECURE-IBD registry, IBD medications were stopped in 518 [34.6%] patients and continued in 981 [65.4%] patients. Baseline characteristics of patients who stopped and did not stop at least one medication are reported in Table 1. On bivariate and multivariable analyses, a diagnosis of ulcerative colitis [UC] or IBD-unspecified [IBD-U] was associated with a lower odds of stopping medication compared with Crohn's disease [CD] (adjusted odds ratio [aOR] 0.6, 95% CI 0.48, 0.75) [Table 2]. Compared with cases from other countries, those from Italy and Brazil were associated with higher odds of stopping IBD medication on bivariate analysis, but this was not significant in the multivariable model. Other demographic variables, physician global assessment of IBD activity, COVID-19 related emergency room visit, or hospitalisation were not associated with stopping IBD therapy in the setting of COVID-19.

When evaluating specific medications, 5-ASA was more likely to be continued [*p* <0.001] whereas anti-tumour necrosis factor [anti-TNF] therapy and immunomodulator therapy 96-mercaptopurine [6MP], azathioprine, methotrexate) were more likely to be stopped [global *p* <0.001] [Figure 1]. Of 156 patients on combination therapy with an anti-TNF and an immunomodulator, the anti-TNF alone was stopped in 10 [6.4%], immunomodulator alone in 33 [21.2%], and both medications in 53 [34%] patients. Sixty [38%] patients continued on combination therapy.

4. Discussion

In this brief report, we describe physician practice patterns in holding IBD medications, in an international registry of IBD patients with confirmed COVID-19. IBD medications were more likely to be continued in those with UC or IBD-U than with CD. This is likely due, at least in part, to a higher proportion of UC patients on 5-ASA therapy, which was the most likely medication to be continued. Conversely, anti-TNFs and immunomodulators, used alone or in combination, were the most frequently stopped classes of medications. These practice patterns are largely concordant with expert guidance on IBD medication management in setting of COVID-19.¹

However, IBD medications were continued for nearly two-thirds of patients, and combination therapy with an anti-TNF and immunomodulator in nearly 40% of patients. It is important to note that biweekly or less frequent dosing of certain biologics could affect decision and feasibility to stop. Emergency room visit or hospitalisation due to COVID-19 did not impact on IBD medication management. Although variation in the discontinuation of IBD medications was significant by country in bivariate analyses, these associations did not remain statistically significant in a multivariable model. Notable trends that may have been limited by sample size include lower odds of medication discontinuation in patients from Italy and higher odds of discontinuation in patients from Brazil. These findings suggest the need to further study international variation in practice patterns and patient outcomes. In the absence of these data, we suggest following guidance laid out per expert consensus.¹

Strengths of this study include the use of a large, international registry with a diverse adult and paediatric IBD patient population. Limitations include the considerable risk of reporting bias in this voluntary registry of IBD patients with COVID-19 patients. Another limitation is missing data, although this was <4% for all variables except ethnicity. In the present study, we were not able to evaluate

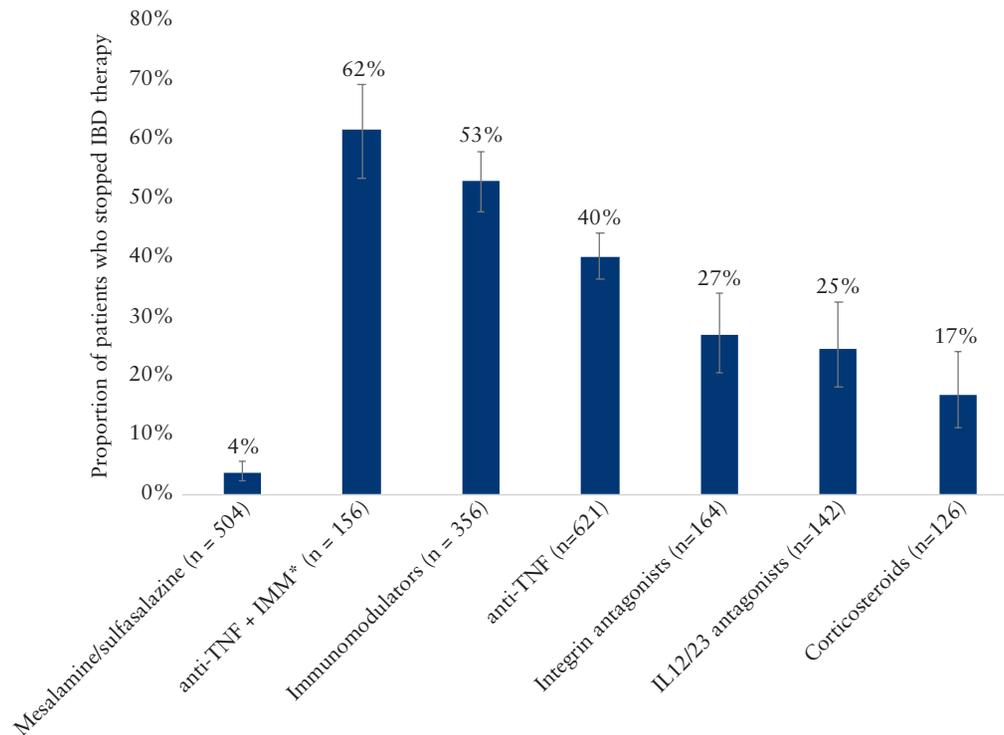


Figure 1. Prescription practice in the setting of COVID-19 based on IBD medication class*. Medication categories are not mutually exclusive unless otherwise noted. *At time of COVID-19 infection; *stopping either anti-TNF, IMM, or both. TNF = tumour necrosis factor; IMM, immunomodulator; IL, interleukin.

the impact of holding or continuing medications on COVID-19 outcomes, due to issues related to unmeasured confounding of COVID-19 severity and lack of data regarding duration of holding medication and timing of medication restarting.

In summary, we found that IBD medications other than immunomodulators were continued in the majority of IBD patients with COVID-19, in the international SECURE-IBD registry. Future studies are needed to understand the impact of stopping or continuing IBD medications on IBD-related outcomes as well as COVID-19 related outcomes. The data underlying this article are available in the article and in its online supplementary material.

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Conflict of Interest

The corresponding author confirms on behalf of all authors that there have been no involvements that might raise the question of bias in the work reported or in the conclusions, implications, or opinions stated. MA receives research support from the Dickler Family Fund, New York Community Trust, and Helmsley Charitable Trust Fund for SECURE-IBD. EJB is supported by an Institutional Training Grant from the National Institutes of Health [T32DK007634]. JFC reports receiving research grants from AbbVie, Janssen Pharmaceuticals, and Takeda; receiving payment for lectures from AbbVie, Amgen, Allergan, Ferring Pharmaceuticals, Shire, and Takeda; receiving consulting fees from AbbVie, Amgen, Arena Pharmaceuticals, Boehringer Ingelheim, Celgene Corporation, Celltrion, Eli Lilly, Enterome, Ferring Pharmaceuticals, Genentech, Janssen Pharmaceuticals, Landos, Ipsen, Medimmune, Merck, Novartis, Pfizer, Shire, Takeda, Tigenix, and Viela bio; and holds stock options in Intestinal Biotech Development and Genfit. MDK has consulted for Abbvie, Janssen, Pfizer, and Takeda, is a shareholder in Johnson & Johnson, and has received research

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Author Contributions

MA: study concept and design, interpretation of data, drafting of manuscript, critical revision of the manuscript for important intellectual content; EJB: study concept and design, acquisition of data, interpretation of data, critical revision of the manuscript for important intellectual content; XZ: acquisition, analysis, and interpretation of data; JFC: study concept and design, interpretation of data, critical revision of the manuscript for important intellectual content; MDK: study concept and design, interpretation of data, critical revision of the manuscript for important intellectual content; RCU: study concept and design, acquisition of data, interpretation of data, critical revision of the manuscript for important intellectual content.

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References

- Rubin DT, Abreu MT, Rai V, Siegel CA. Management of patients with Crohn's disease and ulcerative colitis during the coronavirus disease-2019 pandemic: results of an International Meeting. *Gastroenterology* 2020;159:6-13.
- Brenner EJ, Ungaro RC, Geary RB, *et al*. Corticosteroids, but not TNF antagonists, are associated with adverse COVID-19 outcomes in patients with inflammatory bowel diseases: results from an International Registry. *Gastroenterology* 2020. PMID: 32425234.