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Mesalazine in Inflammatory Bowel Disease and COVID-19: Hospitalization and Adverse In-Hospital Outcomes Based on Nationwide Data

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Background. We assessed whether 5-aminosalicylic acid (5-ASA), as treatment for inflammatory bowel disease (IBD), was associated with an increase in hospitalization for coronavirus disease 2019 and adverse in-hospital outcomes.

Methods. This was a Danish nationwide register study. The study population consisted of all patients with an IBD diagnosis between March 1, 2010, and March 1, 2020, and living in Denmark on March 1, 2020. Patients with IBD treated with 5-ASA (exposed) were compared with patients not receiving 5-ASA (unexposed).

Results. We identified 60 242 patients with IBD; 15 635 (40.5%) with ulcerative colitis (UC) and 964 (4.5%) with Crohn's disease (CD) were exposed to 5-ASA. For patients with UC who were 5-ASA exposed, the hazard ratio of hospitalization was 1.18 (95% confidence interval, 0.79-1.78). In-hospital outcomes were not statistical significant from those not exposed to 5-ASA (median length of hospital stay 5.6 days vs 7.2 days), mechanical ventilation (0% vs 14%), continuous positive airway pressure (7.9% vs 9.4%), and in-hospital mortality (21.1% vs 17.2%). For patients with CD, the hazard ratio of hospitalization was 2.25 (95% confidence interval, 1.02-4.97). We found no statistically significant difference in length of hospital stay (7.1 days vs 3.9 days), mechanical ventilation (0% vs 1.8%), use of continuous positive airway pressure (0% vs 1.8%), or in-hospital mortality (0% vs 9%) between exposed and unexposed patients.

Conclusions. Patients with UC, treated with 5-ASA, had no increased risk of hospitalization for coronavirus disease 2019 or more adverse in-hospital outcomes. In patients with CD, 5-ASA may be associated with an increased risk of hospitalization but not with more adverse in-hospital outcomes.

Lay Summary

In this national register study, 5-aminosalicylic acid (5-ASA)–treated ulcerative colitis patients had no increased risk of hospitalization for coronavirus disease 2019 (COVID-19) or more adverse in-hospital outcomes compared with patients not treated with 5-ASA. Also, 5-ASA–treated patients with Crohn's disease did not have more adverse in-hospital outcomes.

Key Words: COVID-19, inflammatory bowel disease, mesalazine

Introduction

In December 2019, the first report of a new cluster of pneumonia cases emerged from the Chinese province of Wuhan.[1] By January 2020, a novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was isolated from infected patients, and the disease was named coronavirus disease 2019 (COVID-19). Two months later, on March 11, the World Health Organization declared the disease a pandemic, as it had spread to over 118 000 people in over 114 countries and resulted in 4291 deaths.[2] Since then, the number has only been increasing, and as of April 2021, an estimated 131 million people had been infected and 2.8 million had died worldwide.[3]

The earliest case reports from January 2020 described COVID-19 as having a heterogenic disease course ranging from mild upper airway infection to severe acute respiratory syndrome necessitating oxygen support, invasive mechanical ventilation, and admission to intensive care units (ICUs), but even then with a potentially fatal outcome.[4] The rapid spread of COVID-19 combined with potentially severe disease course has caused an urgent need for knowledge on how to manage the virus. Admirable progress has been made in developing vaccines counteracting the virus, but identifying groups at risk of a severe outcome is still essential for ensuring optimal care and prioritization of vaccines.[5-8]

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While high age, hypertension, diabetes, chronic obstructive pulmonary disease, cardiovascular disease, and cerebrovascular disease have all been shown to be independent risk factors for adverse outcomes due to COVID-19 infection,[9-13] inflammatory bowel disease (IBD) as a risk factor is still a matter of discussion. While it does not seem that IBD in itself constitutes an increased risk of infection or adverse effect of coronavirus compared with the general population,[14-17] some studies have found that IBD patients treated with systemic glucocorticoids have an increased risk of COVID-19 and severe disease course.[18,19] In patients with IBD, anti-tumor necrosis factor α (anti-TNF-α) therapy do not seem to have a negative impact on hospitalization or death.[9,14] One study even found anti-TNF-α monotherapy to have a possible protective effect against developing a severe COVID-19 infection, relative to other IBD therapies.[20] The same study raised the question whether patients with IBD receiving 5-aminosalicylic acid (5-ASA) treatment had an increased risk of adverse outcome (defined by a composite endpoint of ICU admission, mechanical ventilation, and/or death) following COVID-19.[20] Another large retrospective study could not document increased risk of COVID-19 or worse outcome in IBD patients treated with 5-ASA, although it should be noted that this study's cohort primarily consisted of male individuals with a high mean age.[19]

Thus, this population-based study aims to uncover whether 5-ASA constitutes an increased risk of COVID-19 hospitalization for IBD patients, and whether 5-ASA is associated with an increased risk of adverse in-hospital outcomes.

Methods

All Danish citizens (total population approximately 5.8 million) have access to a tax-supported and uniformly organized health care system. Furthermore, all Danish citizens are assigned a unique civil registration number at birth or immigration, making linkage across various Danish registries possible and valid. We used the Danish National Patient Registry (DNPR)[21] and the Danish Central Personal Registration (CPR) system [22] to create a cohort of IBD patients and supplemented the cohort with information on filled prescriptions from the Danish National Prescription Registry.[23]

The DNPR consists of data on all discharges from the Danish hospital system from 1977 and all outpatient visits since 1994 and onward. Basic data include information on hospitals, departments, surgeries and procedures performed, AND diagnoses given at the hospitals, along with date and time of admission and discharge. All diagnostic codes from 1977 to the end of 1993 are coded according to the Danish version of the International Classification of Diseases–Eighth Revision, and since 1994 according to International Classification of Diseases–Tenth Revision (ICD-10). The Central Personal Registration system is a highly accurate registry, containing information on sex, age, deaths, and immigration since 1968.

We created a cohort of all patients who had an IBD diagnosis (Crohn's disease [CD] ICD-10: K50*; or ulcerative colitis [UC] ICD-10: K51*) between March 1, 2010, and March 1, 2020, and who were living in Denmark on March 1, 2020. We followed the cohort until either a COVID-19–related hospitalization, emigration, death, or end of follow-up on February 28, 2021.

Definition of Exposure

Exposure to 5-ASA was based on filled prescriptions from the Danish National Prescription Registry, which contains data from 1994 and onward.[23] The registry provides information on all filled prescriptions in pharmacies in Denmark. Information comprises the type of medication, classified according to the Anatomical Therapeutic Chemical (ATC) classification system, as well as the place and time of redemption.

Exposure to 5-ASA (ATC: A07EC) was constructed as a time-varying variable for each individual patient. To construct the variable, we used prescriptions issued after March 1, 2019 (1 year before the start of the pandemic in Denmark), until February 28, 2021 (end of follow-up). Patients needed a minimum of 2 prescriptions to be considered as exposed, and the start of exposure was calculated from the date of the second filled prescription. We chose to use a minimum of 2 prescriptions of 5-ASA to ensure that exposed patients were actual users of 5-ASA. After filling a prescription of 5-ASA, a patient was exposed for 6 months. If a patient filled another prescription during this period, this prescription was considered to be part of the same exposure window, and the patient remained exposed until 6 months after the new prescription, and so forth. If a patient did not fill a new prescription within the 6-month window, the patient was regarded as unexposed again. A patient could then come under exposure again if they filled a new prescription of 5-ASA. Thus, patients could be both exposed and unexposed during the study period and have more than 1 exposure window during this period.

When examining adverse in-hospital outcomes for the patients admitted to the hospital for COVID-19, patients were considered exposed if they were exposed to 5-ASA on the day of admission in the first part of this study (ie, the patient had filled a prescription within 6 months of admission).

Outcomes

Outcomes were based on discharge diagnoses, administrative and procedure codes from the DNPR, and mortality data from the CPR system.

Hospitalizations for COVID-19 (yes/no) in the period from March 1, 2020, until February 28, 2021, were retrieved from the DNPR. All outcomes were based on hospitalizations, and we only included those patients who had a COVID-19 diagnostic code as the primary reason for the hospitalization (COVID-19 infection without localization, ICD-10: B342A; or COVID-19 with severe respiratory syndrome, ICD-10: B972A) and in which the patient had a hospital contact with a duration of at least 12 hours.[24] If a patient had more than 1 hospitalization for COVID-19, the outcome was only calculated according to the date of the first hospitalization for COVID-19.

The length of hospital stay was defined as the total time in hospital from admission to discharge. Patients who received continuous positive airway pressure (CPAP) or mechanical ventilator treatment had a respective procedure code during their admission for COVID-19 according to CPAP (procedure code: BGFC32) and according to mechanical ventilator treatment (procedure code: BGDA0). In-hospital death was registered and 14-day mortality was defined as death within 14 days after discharge.

Data on Confounders

Covariates were selected a priori. From the CPR system, we retrieved data on the sex and age of each person on March 1, 2020.

From the DNPR, we obtained data on comorbid diseases for the study population and we calculated the Charlson Comorbidity Index (CCI) based on data 10 years back from March 1, 2020.[25] The index covers 19 major disease categories weighted according to their prognostic impact, and 3 index levels were defined: no comorbidity (CCI score 0), moderate comorbidity (CCI score 1-2), and severe comorbidity (CCI score 3+).

Exposure to medications, thiopurines (ATC: L04AX01 and L01B B02), methotrexate (ATC: L04AX03 and L01B A01), systemic corticosteroids (ATC: H02AB02, H02AB04, H02AB06, H02AB07 and H02AB09), anti-TNF-α agents (ATC: L04AB and treatment code BOHJ18A), anti-interleukin therapeutic agents (ATC: L04AC and treatment code BOHJ18B), selective immunosuppressive agents including Janus kinase inhibitors (ATC: L04AA and treatment code BOHJ28), and cyclosporine or tacrolimus (ATC: L04AD and treatment code BOHJ20/21), was based on prescriptions and procedure codes, and was constructed as a time-varying variable in the same manner as the exposure to 5-ASA.

Statistical Analysis and Confounders

We constructed tables for the main descriptive variables, sex, age category (≤19, 20-39, 40-59, 60-79, and ≥80 years of age), CCI, and exposure to medications during the study period for the entire IBD cohort, as well as for patients with UC and CD. All results are reported as exact numbers and with proportions in percentages.

We performed a Cox proportional hazards regression analyses separately for UC and CD, using exposure to 5-ASA as a time-varying covariate. March 1, 2020, was used as the entry date (start of the pandemic in Denmark), and thus only time after this date contributed to the model. We estimated crude and adjusted hazard ratios (HRs) for being hospitalized with COVID-19 among exposed patients (5-ASA–exposed patient with IBD) vs nonexposed patients (non–5-ASA–exposed patient with IBD). We used 2 adjusted models: model 1 was adjusted for use of corticosteroids and model 2 was adjusted for use of corticosteroids, age, sex, and CCI. Owing to the insufficient number of outcomes, it was not possible to adjust for any of the other medications. All HRs were reported with 95% confidence intervals (CIs).

Hospital outcomes were presented in contingency tables for exposed and nonexposed, separately for UC and CD. Length of hospital stay was presented with median and interquartile range, and the distribution in exposed vs nonexposed was compared using Wilcoxon's rank sum test.

Table 1. Characteristics of Study Population: Patients Living in Denmark on March 1, 2020, With an IBD Diagnosis Between March 1, 2010, and March 1, 2020

	Patients With IBD (N = 60 242)[a]	Patients With CD (n = 21 547)	Patients With UC (n = 38 589)
Age by January 1, 2020, y	50 (36-64)	46 (32-60)	53 (39-66)
Patient's age category			
≤19 y	1748 (2.9)	976 (4.5)	765 (2.0)
20-39 y	16 296 (27.1)	7107 (33.0)	9156 (23.7)
40-59 y	22 531 (37.4)	7934 (36.8)	14 557 (37.7)
60-79 y	16 387 (27.2)	4709 (21.9)	11 655 (30.2)
≥80 y	3280 (5.4)	821 (3.8)	2456 (6.4)
Sex			
Female	32 740 (54.3)	12 217 (56.7)	20 466 (53.0)
Male	27 502 (45.7)	9330 (43.3)	18 123 (47.0)
Charlson comorbidity index			
0	42 539 (70.6)	15 349 (71.2)	27 113 (70.3)
1-2	13 441 (22.3)	4737 (22.0)	8682 (22.5)
3+	4262 (7.1)	1461 (6.8)	2794 (7.2)
Type of IBD			
CD	21 547 (35.8)	—	—
UC	38 589 (64.1)	—	—
Both diagnosis	106 (0.2)	—	—
Medication exposure during March 1, 2020, to February 28, 2021[b]			
5-ASA	16 625 (27.6)	964 (4.5)	15 635 (40.5)
Thiopurines	3510 (5.8)	1900 (8.8)	1601 (4.1)
Methotrexate	592 (1.0)	293 (1.4)	299 (0.8)
Systemic corticosteroids	4748 (7.9)	1627 (7.6)	3106 (8.0)
Anti-TNF-α agents	5299 (8.8)	3427 (15.9)	1859 (4.8)
Anti-interleukin therapeutic agents	57 (0.1)	19 (0.1)	38 (0.1)
Selective immunosuppressive agents	420 (0.7)	328 (1.5)	90 (0.2)
Ciclosporin/tacrolimus	38 (0.1)	11 (0.1)	26 (0.1)

Values are median (interquartile range) or n (%).
Abbreviations: 5-ASA, 5-aminosalicylic acid; CD, Crohn's disease; IBD, inflammatory bowel disease; TNF-α, tumor necrosis factor α; UC, ulcerative colitis.
[a]A total of 106 were registered with diagnoses of both UC and CD.
[b]Time-varying exposures. Patients can have used medication in more than 1 of these categories in the exposure window.

Use of respirator, CPAP, death during hospitalization, and death within 14 days after discharge was presented with exact number and percentages, and exposed vs nonexposed was tested using Fisher's exact test. Owing to insufficient number of outcomes, it was not possible to do any sensible adjusted analyses.

No power calculation was performed, as we used all available nationwide data and as there were no a priori data on the risk conferred to 5-ASA in relation to the disease course of COVID-19. All calculations were performed using Stata release 16.1 (StataCorp, College Station, TX, USA).

Results

Patient Demographics

We identified 60 242 patients with a diagnosis of IBD before March 1, 2020. Of these, 21 547 patients had CD, 38 589 patients had UC, and 106 patients had been registered with both CD and UC diagnoses (Table 1). Of the 60 242 patients with IBD, a total of 16 625 (27.6%) patients with IBD had received 5-ASA treatment. When divided according to type of IBD, 15 635 (40.5%) of the patients with UC received 5-ASA, 964 (4.5%) of the patients with CD received 5-ASA, and 26 (24.5%) of the 106 patients with both diagnoses received 5-ASA.

The exposed patients with UC receiving 5-ASA contributed with 13 283.1 years' time at risk, and the unexposed patients with UC contributed with 24 870.0 years to the analysis. The patients with UC had a median age of 53 years, and 2794 (7.2%) had a CCI score of 3 or more. The 2 most commonly used treatments for patients with UC were 5-ASA, as mentioned previously, and systemic corticosteroids (n = 3106 [8.0%]). For patients with CD, the time at risk was 756.9 years for the exposed and 20 552.2 years for the unexposed. Patients with a diagnosis of CD had a median age of 46 years, and 1481 (6.8%) had a CCI score of 3 or more. The 2 most common treatments for CD patients were anti-TNF-α therapy and thiopurines: 3427 (15.9%) and 1900 (8.8%), respectively.

Hospitalization

Table 2 shows the crude HR and the adjusted HR (models 1 and 2) for hospitalization with COVID-19 according to use of 5-ASA, relative to patients not treated with 5-ASA, and stratified according to UC or CD diagnoses. Among patients with UC, 102 were admitted to hospital due to COVID-19 from the March 1, 2020, to February 28, 2021. A total of 38 were admitted while exposed to 5-ASA, and 64 were unexposed to 5-ASA. The crude HR for hospitalization of UC patients treated with 5-ASA was 1.11 (95% CI, 0.75-1.66). HRs according to models 1 and 2 were 1.01 (95% CI, 0.67-1.51) and 1.18 (95% CI, 0.79-1.78), respectively (Table 2). Among patients with CD, 63 were admitted to hospital due to COVID-19, and of these, 7 were hospitalized while exposed to 5-ASA, while 56 were unexposed to 5-ASA. The crude HR for hospitalization of CD patients treated with 5-ASA was 3.37 (95% CI, 1.54-7.39). When adjusting for potential confounders, the HR decreased, and the HR for hospitalization in model 2 was 2.25 (95% CI, 1.02-4.97). A graphic presentation of these results is shown in Figure 1.

Hospital Outcome

Table 3 shows adverse hospital outcomes for patients treated with 5-ASA compared with patients not treated with 5-ASA, stratified according to UC and CD.

For patients with UC, no statistically significant difference was found between the 2 groups with regard to length of hospital stay, use of CPAP treatment, and death in hospital or 14 days after hospital discharge. Interestingly, while no patients with UC treated with 5-ASA received mechanical ventilation, 9 patients with UC not treated with 5-ASA received mechanical ventilation ($P = .04$).

For patients with CD, no statistically significant difference was found between the 2 groups with regard to length of hospital stay, mechanical ventilation, use of CPAP treatment, and death at the hospital or 14 days after hospital discharge.

Discussion

This is, to our knowledge, the largest unselected population-based study examining the association between 5-ASA treatment and outcomes of COVID-19 infection in patients with IBD to date, and as such, this study has several strengths. In a recent study, Ungaro et al[20] suggested an increased risk of severe COVID-19 in relation to mesalazine or sulfasalazine and suggested that this finding should be confirmed in large population cohorts.

Table 2. The Crude and Adjusted HRs for Hospitalization with COVID-19 According to Exposure to 5-ASA With Corresponding 95% CI, Relative to Patients Not Treated with 5-ASA: Hospitalizations for COVID-19 From March 1 to February 28, 2021

	Number of Events	Total Time at Risk (y)	Crude HR	95% CI	Model 1		Model 2	
					Adjusted HR[a]	95% CI	Adjusted HR[b]	95% CI
Ulcerative colitis								
Exposed cohort	38	13 283.1	1.11	0.75-1.66	1.01	0.67-1.51	1.18	0.79-1.78
Unexposed cohort	64	24 870.0						
Crohn's disease								
Exposed cohort	7	756.9	3.37	1.54-7.39	3.07	1.40-6.78	2.25	1.02-4.97
Unexposed cohort	56	20 552.2						

Abbreviations: 5-ASA, 5-aminosalicylic acid; CI, confidence interval; COVID-19, coronavirus disease 2019; HR, hazard ratio.
[a]Adjusted for corticosteroids.
[b]Adjusted for corticosteroids, sex, age, and Charlson Comorbidity Index.

Thus, we found that patients with UC treated with 5-ASA did not have an increased risk of hospitalization or worse in-hospital outcomes or death, compared with patients with UC not receiving 5-ASA. Although we found an increased risk of hospitalization among patients with CD treated with 5-ASA, this group, however, did not have worse in-hospital outcome or death compared with patients with CD not receiving 5-ASA.

Large case studies and retrospective cohort studies have produced contradicting results regarding the risk for COVID-19 and the outcome in IBD patients treated with 5-ASA.[19,20,26,27] An international registry study of patients with UC and CD by Ungaro et al[20] found an increased risk of severe COVID-19 outcome (composite endpoint of ICU admission, mechanical ventilation, and/or death) when comparing mesalazine or sulfasalazine use with no use of these medications or comparing mesalazine or sulfasalazine usage with anti-TNF-α monotherapy. The adjusted ratios for said comparisons were 1.70 (95% CI, 1.26-2.29) and 3.52 (95% CI, 1.93-6.45), respectively.[20] In contrast to Ungaro et al, we did not find an increase of adverse in-hospital outcomes when examining use of 5-ASA in patients with UC—we also found no increase in hospitalization. In another study—consisting primarily of males (Veterans Affairs Healthcare System)—mesalazine was also not associated with an increased risk of SARS-CoV-2 or severe COVID-19 (combined endpoint of hospitalization or death) in patients with UC and CD, compared with other medications for IBD or with no medications.[19] Also, in Danish cohort studies of patients with UC and CD, no association between 5-ASA use and severe COVID-19 outcome could be demonstrated.[26,27]

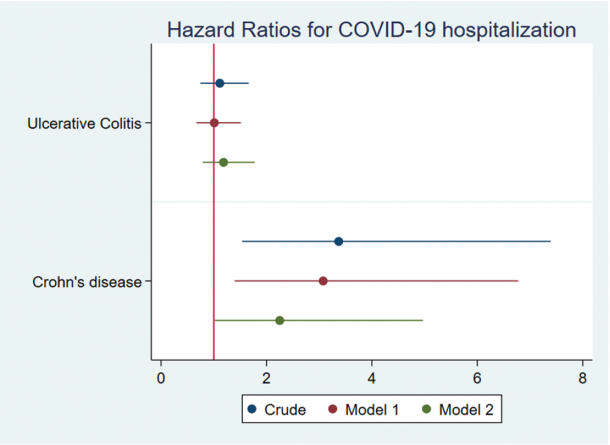

Figure 1. Coefficient plot showing crude hazard ratio and hazard ratio adjusted according to models 1 and 2, respectively. The dots represent the point estimate and the lines represents the confidence interval. The analysis is stratified by ulcerative colitis or Crohn's disease. COVID-19, coronavirus disease 2019.

In our study, the finding of an increased risk of hospitalization due to COVID-19 infection in patients with CD receiving 5-ASA was not expected. However, this increased risk should be interpreted with caution. The risk of hospitalization in patients with CD receiving 5-ASA was examined in crude analysis and across 2 different adjusted regression models, and the more possible confounders we included in the model, the more the risk estimate approached the null hypothesis. Therefore, an impact of unadjusted confounding cannot be ruled out. However, importantly, the use of 5-ASA in patients with CD was not associated with worse in-hospital outcomes, compared with patients with CD not receiving 5-ASA.

Generally, 5-ASA treatment does not hold a place in treatment of CD—neither for induction nor for maintenance of remission—as most meta-analyses on the subject find that 5-ASA has a sparse effect on inducing remission of CD and maintaining remission.[28-31] The increased risk of severe COVID-19 outcome in 5-ASA–exposed patients in the study by Ungaro et al[20] was also present when restricting analysis to either CD or UC. In the study by Khan et al,[19] the analysis was not done specifically on patients with CD, but in a further analysis on the Danish cohort study, no association to severe outcome was found when stratifying for CD or UC.[26]

Table 3. Median Length of Hospital Stay and Hospital Outcomes for Patients Exposed to and Not Exposed to 5-ASA Stratified by Ulcerative Colitis or Crohn's Disease)

	Exposed to 5-ASA	Unexposed	*P* Value
Ulcerative colitis	n = 389	n = 64	
Length of hospital stay, d	5.6 (3.8-13.7)	7.2 (2.7-12.2)	.98[a]
Ventilator	0 (0.0)	9 (14.0)	.04[b]
CPAP	3 (7.9)	6 (9.4)	.55 [b]
Death	8 (21.1)	11 (17.2)	.31 [b]
Death 14 d	10 (26.3)	10 (18.8)	.15 [b]
Crohn's disease	n = 7	n = 56	
Length of hospital stay, d	7.1 (4.0-11.3)	3.9 (1.6-8.1)	.14 [a]
Ventilator	0 (0.0)	1 (1.8)	.89 [b]
CPAP	0 (0.0)	1 (1.8)	.89 [b]
Death	0 (0.0)	5 (9.0)	.54 [b]
Death 14 d	1 (14.3)	7 (12.5)	.63 [b]

Values are median (interquartile range) or n (%).
Abbreviations: 5-ASA, 5-aminosalicylic acid; CPAP, continuous positive airway pressure.
[a]Wilcoxon rank sum test.
[b]Fisher's exact test.

An important difference between our study and the large study by Khan et al[19] was that the current study population was based on unselected nationwide Danish data, and therefore our study population included both men and women with IBD, whereas Khan et al included 91% men. Also an important difference is that the median age was as high as 71 years in the study by Khan et al, whereas in the current study the median age was 53 and 46 years for UC and CD, respectively. Furthermore, information about events and prescriptions filled outside Veterans Affairs Healthcare System may not have been included in the Khan et al study. Finally, the outcome in our study included various outcomes of hospitalization related to COVID-19 infection and COVID-19–related mortality.

As the study was based on 2 Danish registries encompassing the entire Danish population, the DNPR and the CPR, all patients diagnosed with IBD were automatically included in the cohort, thus eliminating geographical and reporting bias. The study design secured a full follow-up of all patients, and thus we have no selection bias. Also, our outcome data were obtained independently of the hypotheses investigated and of exposure assessment, which prevents differential misclassification of the outcome measurements. The study also has limitations. We could not guarantee adherence to the prescribed medical therapies with 5-ASA, but we practically eliminated a potential risk of misclassification of drug exposure by our requirement of a minimum of 2 filled prescriptions for each patient. A weakness of this study was our inability to perform adjusted analyses according to adverse in-hospital outcomes. This was due to few 5-ASA exposed hospitalized patients and, fortunately, only few adverse in-hospital outcomes. The ability to perform adjusted analyses is likely to be improved in future studies as more cases of hospitalizations and adverse in-hospital outcomes will emerge. This will hopefully confirm the safety of 5-ASA treatment in IBD also in relation to SARS-CoV-2.

In conclusion, in this register study we found no evidence suggesting that patients treated with 5-ASA for UC had an increase in either hospitalization or worse in-hospital outcomes due to COVID-19 infections, compared with patients with UC not receiving 5-ASA. We did find evidence to suggest that patients treated with 5-ASA for CD had an increased risk of hospitalization, but the result should be interpreted with caution. As for patients with UC, we did not find worse in-hospital outcomes in patients with CD treated with 5-ASA. These findings are reassuring for patients receiving and physicians prescribing 5-ASA, as 5-ASA still is the first-choice therapy for mild to moderate UC,[29] and our data suggest that 40% of patients with UC receive this treatment option.

Acknowledgments

This study followed all currently applicable Danish laws regarding scientific research. According to Danish law, no ethical approvals of register-based studies are necessary. The study was approved by the Danish Data Protection Agency (j.nr. 20/16376). The use of these register data has been approved for use in this study but does not allow us to distribute or share the patient data with other parties. Access to the data can be achieved through an application to the Research Service at the Danish Health Data Authority (forskerservice@sundhedsdata.dk) should any researchers feel so inclined. Access to data from the Danish Health Data Authority requires approval form the Danish Data Protection Agency. The authors do not have special access privileges to the data used in the current study.

Group Study Participants

Patient representatives are part of the research council at our department, and patient representatives have been involved in the process of this study.

Author Contributions

S.K.: Assistance with data analysis, interpretation of results, manuscript writing and editing, approved the final version. B.M.N.: funding, conception, design, assistance with data analysis, interpretation of results, manuscript writing and editing, approved the final version. J.N.: conception, design, data collection, data analysis, interpretation of results, manuscript editing, approved the final version. J.K.: funding, conception, design, assistance with data analysis, interpretation of results, manuscript writing and editing, approved the final version.

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Conflicts of Interest

There are no competing interests for any of the authors.

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