HHS Public Access

Author manuscript

Curr Opin Gastroenterol. Author manuscript; available in PMC 2022 July 01.

Published in final edited form as:

Curr Opin Gastroenterol. 2021 July 01; 37(4): 313–319. doi:10.1097/MOG.0000000000000741.

Optimal Inflammatory Bowel Disease Management During the Global COVID-19 Pandemic

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Abstract

Purpose of review—This review aims to summarize the current evidence regarding the risks and implications of coronavirus disease 2019 (COVID-19) in patients with inflammatory bowel disease (IBD) and discuss optimal management of IBD during this pandemic.

Recent findings—Patients with IBD are not at increased risk of COVID-19, but several risk factors for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2 infection) have been identified such as active IBD, obesity, and corticosteroid use. COVID-19 outcomes are similar among patients with IBD and the overall population. Although biologics have not been shown to increase the risk of severe COVID-19 complications, several risk factors have been associated with negative COVID-19 outcomes in patients with IBD, including older age, obesity, the presence of comorbidities, active disease and corticosteroid use. IBD therapy should therefore be continued with the aim of attaining or maintaining remission, except for corticosteroids which should be held or reduced to the minimal effective dose. Although it has been recommended that immunosuppressive therapy be held during a case of COVID-19, the half-lives of these drugs and data on the timing of restarting therapy limit the strength of these recommendations. We recommend COVID-19 vaccination for IBD patients when available, as benefits to the individual and to society outweigh the risks.

Summary—As our understanding of SARS-CoV-2 and COVID-19 continues to evolve, we are learning more about its impact in patients with IBD and how to better manage patients in this setting. Managing IBD during this pandemic has also highlighted the importance of restructuring services in order to adapt to current and potential future outbreaks. The COVID-19 pandemic has

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Conflicts of interest and potential competing interests: FR is on the advisory board or consultant for Agomab, Allergan, AbbVie, Boehringer-Ingelheim, Celgene, CDISC, Cowen, Genentech, Gilead, Gossamer, Guidepoint, Helmsley, Index Pharma, Janssen, Koutif, Metacrine, Morphic, Pfizer, Pliant, Prometheus Biosciences, Receptos, RedX, Roche, Samsung, Takeda, Techlab, Theravance, Thetis, UCB. SE has no conflict of interest.

transformed IBD care through the expansion of telemedicine and development of novel approaches to remote monitoring.

Keywords

COVID-19; SARS-CoV-2; inflammatory bowel disease; Crohn's disease; ulcerative colitis

Introduction

As the world continues to grapple with the Coronavirus disease 2019 (COVID-19) pandemic, our understanding of the disease and its impact on our patients with inflammatory bowel disease (IBD) is evolving. The pandemic has had a considerable impact on patients with IBD and their care (1). Beyond the important influence on psychosocial aspects of patients (2), many other parts of their care have been affected (1). In addition to a significantly reduced access to endoscopy, surgery and laboratory testing (1, 3), there have been extensive changes in the delivery of care in order to adapt to the pandemic through increased use of telemedicine and remote monitoring (4). In this review we provide an up-to-date summary of current evidence regarding the risk of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in patients with IBD and discuss optimal management of IBD during a pandemic.

Risk of SARS-CoV-2 infection in IBD

Based on available evidence to date, patients with IBD are not at increased risk of SARS-CoV-2 infection. Several initial studies from North America, Asia and Europe have found a similar incidence of COVID-19 among patients with IBD compared to the general population (5–9) and this remains the case in most recent literature (10). In a large nationwide Dutch cohort study, the incidence of COVID-19 among patients with IBD and the general Dutch population were found to be similar (10). In a Spanish cohort study the rates of infection among patients with IBD were actually lower than in the general population (6).

While SARS-CoV-2 infection rates are not increased in patients with IBD, several risk factors for infection and specifically development of COVID-19 have been identified in patients with IBD. Obesity, corticosteroids and moderate to severe disease activity were found to be associated with an increased risk of COVID-19 (8, 11). It is important to note that thiopurines and biologics have not been associated with an increased risk of SARS-CoV-2 infection (11, 12).

Clinical manifestations of COVID-19 in IBD

In a systematic review of 23 studies assessing COVID-19 manifestations in 1028 patients with IBD, the most common symptoms were fever, cough, and diarrhea, which were present in 48.3%, 46.5%, and 20.5% of patients, respectively (13). Although gastrointestinal (GI) symptoms have been commonly described in COVID-19 (14), patients with IBD appear to present with GI symptoms more frequently than the general (non-IBD) population (13). Compared to non-IBD matched controls, not surprisingly, patients with IBD reported more frequent abdominal pain and diarrhea with COVID-19 (8). In a Spanish case series, diarrhea

was the predominant presenting symptom in 42% of patients with IBD who developed COVID-19 (6). Importantly for clinical practice, SARS-CoV-2 infection may mimic relapses of IBD in these patients (15). Patients with IBD who developed COVID-19 had an increased risk of abdominal pain, diarrhea, abnormal inflammatory markers (C-reactive protein and fecal calprotectin), as well as active disease on endoscopy as compared with non-infected IBD patients (8). SARS-CoV-2 infection should therefore be considered in any patient presenting with GI symptoms, especially if other typical manifestations of COVID-19 are also present, such as anosmia, dysgeusia, fever or respiratory symptoms (15), and this is particularly true in patients with IBD.

Interestingly, *de novo* IBD has also been described in case reports in the setting of COVID-19. A young, otherwise healthy woman developed chronic bloody diarrhea after documented COVID-19 infection. A colonoscopy performed 5 months after COVID-19 showed left-sided ulcerative colitis and biopsies showed typical features of IBD (16). Distinguishing between COVID-19 and new or relapsing IBD can thus be challenging and requires a thorough clinical evaluation including a careful history, stool studies, endoscopic and histopathologic assessment as well as SARS-CoV-2 testing (15). Although fecal calprotectin can be used, it may not help differentiate between a relapse of IBD and COVID-19. COVID-19 patients presenting with diarrhea do have increased fecal calprotectin levels compared with COVID-19 patients without diarrhea (17), but this is usually in a range of 100–200 mcg/g rather than the much higher levels that may be seen in actively inflamed IBD.

COVID-19 outcomes in patients with IBD

Multiple studies have evaluated the impact of COVID-19 and its complications in patients with IBD and have found similar outcomes compared with the general population (15). Studies from the US (7, 8), Spain (6), France (9), and Italy (9) have all shown comparable findings. In a large IBD cohort study of 34763 patients, 20% of patients who developed COVID-19 had a severe course, as defined by the need for intensive care unit (ICU) admission, mechanical ventilation or death (10). However, rates of COVID-19 complications were found to be similar to a reference population. The presence of one or more comorbidities was found to be independently associated with hospitalization (10). In a systematic review, 30.6% of patients with IBD and COVID-19 required hospitalization, 11.4% required admission to an ICU and 3.8% died. These rates were again found to be similar to the general population (13). The Surveillance Epidemiology of Coronavirus Under Research Exclusion for Inflammatory Bowel Disease (SECURE-IBD) registry has greatly contributed to our current understanding of COVID-19 outcomes in IBD (18). This ongoing global effort has helped collect data on patients with IBD and COVID-19 from 64 countries. As of February 13, 2021, out of 5081 included patients, hospitalization, ICU admission and mortality rates were 16%, 3% and 2%, respectively (18). We strongly encourage our colleagues to enter their patients into this registry in order to expand the understanding of COVID-19 and IBD (18).

Risk factors for severe COVID-19 in IBD

While COVID-19 outcomes are overall similar in patients with IBD and the overall population, several risk factors for severe COVID-19 among patients with IBD have been identified and are listed in Table 1.

Similar to the general population, the presence of comorbidities has been frequently associated with worse outcomes in patients with IBD (10, 19–21). Older age and obesity have also been linked with a more severe course of COVID-19 (11, 19, 20). Furthermore, actively inflamed IBD was found to be associated with severe COVID-19 outcomes in a prospective cohort study, including a higher risk of COVID-19-related death (19). Corticosteroid use has been identified as an important risk factor for negative outcomes in the SECURE-IBD registry (20, 22). Of note, short-term dexamethasone has been shown to improve mortality in patients with severe COVID-19 requiring respiratory support in the RECOVERY trial (23). However, this may be related to the inhibition of the acute cytokine release storm in these patients, whereas baseline corticosteroid use among patients with IBD at the time of infection may potentially negatively impact the future course of COVID-19 (22). The association with corticosteroid therapy and worse COVID-19 outcomes spans beyond just patients with IBD and has also been found in a cohort of patients with other immune mediated diseases (7). In addition, corticosteroids have been previously associated with worse outcomes in patients with other coronavirus outbreaks, the Middle East respiratory syndrome (MERS-CoV) and the first severe acute respiratory syndrome (SARS-CoV, now called SARS-CoV-1) (15).

Finally, an intriguing risk factor identified in the SECURE-IBD registry was 5-aminosalicylate (5-ASA) use, which was associated with an increased risk of severe COVID-19 compared with patients not using 5-ASAs (20, 22). However, patients receiving 5-ASAs were not at increased risk of negative outcomes compared with patients receiving no IBD medications. In addition, no dose-relationship was found (22). Further data are therefore needed in order to clarify whether this is related to unmeasured confounders, such as active IBD or use of 5-ASA for Crohn’s disease, a protective effect of other therapies, or if this is due to a true biologic effect on the enzymes and mode of entry of the coronavirus (24).

IBD therapies and their impact on COVID-19 outcomes

Importantly, the available biologic therapies for IBD have not been associated with worse outcomes from COVID-19 (7, 19, 20, 25). Several biologics are in fact being studied as potential COVID-19 treatment options in ongoing randomized controlled trials, including anti-TNFs (adalimumab, ChiCTR2000030089; infliximab, NCT#04425538) and several Janus kinase inhibitors including tofacitinib (NCT#04469114) (26). Interestingly, infliximab has been successfully used to simultaneously treat COVID-19 and severe IBD in two case reports. The course of COVID-19 in both patients improved significantly after the administration of infliximab (27, 28).

In contrast, in a more recent expanded analysis of the SECURE-IBD registry on 1439 patients from 47 countries, thiopurines were associated with an increased risk of severe

COVID-19 compared with anti-TNF monotherapy, whether alone (adjusted OR (aOR) 4.08, 95% CI 1.73 to 9.61) or in combination therapy with anti-TNFs (aOR 4.01, 95% CI 1.65 to 9.78) (22). Mesalamine was also found to be associated with an increased risk of severe COVID-19 (aOR 1.70, 95% CI 1.26 to 2.29), with a further increased risk when compared to anti-TNF monotherapy (aOR 3.52, 95% CI 1.93 to 6.45). Although these findings suggest thiopurines or mesalamine may be associated with worse outcomes, they may also be due to a potential protective effect of anti-TNFs or unmeasured confounders (29). Further data are therefore needed before changing clinical practice.

Finally, in an analysis of 37 patients on tofacitinib in the SECURE-IBD database, tofacitinib was not associated with an increased risk of severe COVID-19 (30), and there are multiple ongoing studies of tofacitinib as a treatment for COVID-19. Moreover, despite the increased risk of thrombosis associated with COVID-19, there were no reported thrombotic events among patients on tofacitinib (30).

Optimal management of IBD during a pandemic: general recommendations

Many questions arose at the onset of the pandemic regarding the management of patients with IBD. However, several societies came together early on to provide expert opinion-based guidance, due to the initial lack of data on outcomes in IBD (31–33). Although there are some practical issues regarding the half-lives of IBD therapies and recommendations to hold or discontinue them at the time of a SARS-CoV-2 infection or COVID-19, most recommendations are still valid and are in line with the accumulating evidence on IBD and COVID-19 outcomes. A summary of general recommendations can be found in Table 2.

Patients should remain on their maintenance regimen, if in remission, in order to avoid the risk of relapse. The exception is for oral systemic corticosteroids, which should be tapered, reduced to the minimal effective dose or stopped (32, 33). Non-adherence to maintenance therapy may lead to disease relapse, which in turn may be associated with an increased risk of COVID-19 (8), increased corticosteroid use and SARS-CoV-2 exposure through more frequent hospital visits (33). Biologic infusions should be continued at centers with a COVID-19 screening protocol and adequate hygiene and safety standards, as recommended by the International Organization For the Study of Inflammatory Bowel Disease (IOIBD) taskforce (34). De-escalation of therapy doses or discontinuation of therapies otherwise has not been recommended for risk of relapse. Similarly, elective transition from intravenous anti-TNF therapy to an injectable anti-TNF therapy should not be electively performed, as this can be associated with a loss of drug efficacy and tolerance (33, 43).

Although endoscopy remains a crucial diagnostic and monitoring tool in IBD, elective endoscopic procedures have had to be canceled or postponed due to the pandemic, leading to a significant drop in endoscopic volume (1). IOIBD experts have compiled a list of recommendations for IBD endoscopy during the pandemic (37). Procedures should be performed according to adequate safety measures and prioritized according to the urgency of their indication. High priority procedures include acute severe UC, cholangitis in the case of concurrent primary sclerosing cholangitis, partial bowel obstruction, new diagnosis of IBD and acute GI bleeding. If endoscopy if not readily available, fecal calprotectin and serum

inflammatory markers should be used for disease monitoring, in addition to clinical evaluation (37).

Management of the patient with IBD and COVID-19

In the case of SARS-CoV-2 infection, it is generally recommended to hold immunosuppressive therapies (32). However, current recommendations are mostly based on expert consensus and recent evidence does not demonstrate worse outcomes among patients with IBD on biologics, further supported by the fact that the half-lives of these therapies are such that the drugs are still present even with short-term discontinuation. IBD management should therefore be individualized and adapted to the severity of SARS-CoV-2 infection and disease activity (15).

If immunosuppressives are held, IOIBD generally advises to resume therapy at least 10 days after the onset of symptoms and at least 3 days after resolution of fever, once there is "clinically meaningful improvement in respiratory symptoms" (35). However, it is important to note that there are limited data regarding the safety and timing of restarting immunosuppressives after SARS-CoV-2 infection and that other approaches might also be considered, such as a test-based strategy (35). There are case reports suggesting that active therapy for IBD may also address the inflammatory activity of COVID-19, including the rare multi-system inflammatory syndrome in children, and the co-existing active IBD (27, 28, 44).

COVID-19 vaccine and IBD

Several vaccines have been approved for COVID-19 prevention in a number of countries, including mRNA, inactivated, and viral vector-based vaccines (42, 45, 46). Several other vaccines are being investigated in randomized controlled trials and are at different stages of development (47).

Although these non-live vaccines have not been specifically studied in patients with IBD, their safety profile and underlying mechanism suggest they can safely be used in patients with IBD, including immunosuppressed patients (42, 48). Recent IOIBD consensus guidance therefore recommends non-live COVID-19 vaccine administration to all our patients with IBD (42). There are however no data thus far regarding the efficacy of these vaccines in the context of immunosuppression. This should be discussed with patients, especially if they are receiving systemic corticosteroids (42).

Conclusion

The COVID-19 pandemic has had a considerable impact on our patients. As our understanding of COVID-19 and its implications in patients with IBD is evolving, several questions remain regarding the safety of certain therapies such as thiopurines or mesalamine, the timing of restarting therapy after COVID-19 convalescence, as well as regarding the safety and efficacy of COVID-19 vaccines in the patients with IBD. Managing IBD in this context has also led us to appreciate the importance of quickly adjusting to changing norms and restructuring care in order to adapt to future waves or outbreaks. COVID-19 will undoubtedly transform IBD care through the expansion of telemedicine and the development

of point of care testing and novel approaches for remote monitoring, which may in fact benefit our patients in the long-term through access to convenient and safe IBD care well beyond the expected control of the COVID-19 global burden.

Acknowledgments

Grant support: This work was supported by the Helmsley Charitable Trust through the Stenosis Therapy and Anti-Fibrotic Research (STAR) Consortium and National Institutes of Health [K08DK110415 & R01DK123233] to F.R.

Specific author contributions: SE and FR planned and conducted the study. All authors have contributed to drafting and approving the final version of the manuscript.

DTR has received grant support from Takeda; and has served as a consultant for Abbvie, Abgenomics, Allergan Inc., Arena Pharmaceuticals, Bellatrix Pharmaceuticals, Boehringer Ingelheim Ltd., Bristol-Myers Squibb, Celgene Corp/Syneos, Check-cap, Dizal Pharmaceuticals, GalenPharma/Atlantica, Genentech/Roche, Gilead Sciences, Ichnos Sciences S.A., InDex Pharmaceuticals, Iterative Scopes, Janssen Pharmaceuticals, Lilly, Materia Prima, Narrow River Mgmt, Pfizer, Prometheus Laboratories, Reistone, Takeda, and Techlab Inc.

BLC receives the following financial support: Advisory Boards and Consultant for Abbvie, Celgene-Bristol Myers Squibb, Pfizer, Sublimity Therapeutics, TARGET RWE; CME Companies: Cornerstones, Vindico; Speaking: Abbvie MDR is on the advisory board or consultant for Abbvie, Janssen, UCB, Takeda, Pfizer, Miraca Labs, Amgen, Celgene, Seres, Allergan, Genentech, Gilead, Salix, Prometheus, Lilly, TARGET Pharma Solutions, ALFASIGMA, S.p.A., Bristol Meyer Squibb (BMS).

Abbreviations

5-ASA	5-aminosalicylate
AGA	American Gastroenterological Association
Anti-TNF	anti-tumor necrosis factor
CD	Crohn’s Disease
COVID-19	coronavirus disease 2019
GI	gastrointestinal
ICU	intensive care unit
IBD	inflammatory bowel disease
IOIBD	International Organization For the Study of Inflammatory Bowel Disease
MERS-CoV	Middle East respiratory syndrome
mRNA	messenger ribonucleic acid
SARS-CoV	severe acute respiratory syndrome
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
UC	ulcerative colitis

Bibliography

1. Kennedy NA, Hansen R, Younge L, Mawdsley J, Beattie RM, Din S, et al. Organisational changes and challenges for inflammatory bowel disease services in the UK during the COVID-19 pandemic. Frontline Gastroenterology. 2020;11(5):343–50. [PubMed: 32874484]
2. Grunert PC, Reuken PA, Stallhofer J, Teich N, Stallmach A. Inflammatory Bowel Disease in the COVID-19 Pandemic - the Patients' Perspective. J Crohns Colitis. 2020:jjaa126.
3. Shields S, Dunlop A, Seenan JP, Macdonald J. Disease monitoring of biologic treatment in IBD: early impact and future implications of COVID-19 pandemic. Frontline Gastroenterology. 2020:flgastro-2020–101563.
4. Lees CW, Regueiro M, Mahadevan U, International Organization for the Study of Inflammatory Bowel D. Innovation in Inflammatory Bowel Disease Care During the COVID-19 Pandemic: Results of a Global Telemedicine Survey by the International Organization for the Study of Inflammatory Bowel Disease. Gastroenterology. 2020;159(3):805–8.e1. [PubMed: 32474119]
5. Mak JWY, Weng M-T, Wei SC, Ng SC. Zero COVID-19 infection in inflammatory bowel disease patients: Findings from population-based inflammatory bowel disease registries in Hong Kong and Taiwan. Journal of Gastroenterology and Hepatology.n/a(n/a).
6. Taxonera C, Sagastagoitia I, Alba C, Mañas N, Olivares D, Rey E. 2019 novel coronavirus disease (COVID-19) in patients with inflammatory bowel diseases. Alimentary pharmacology & therapeutics. 2020;52(2):276–83. [PubMed: 32359205]
7. Haberman R, Axelrad J, Chen A, Castillo R, Yan D, Izmirly P, et al. Covid-19 in Immune-Mediated Inflammatory Diseases — Case Series from New York. New England Journal of Medicine. 2020;383(1):85–8.
8. Lukin DJ, Kumar A, Hajifathalian K, Sharaiha RZ, Scherl EJ, Longman RS, et al. Baseline Disease Activity and Steroid Therapy Stratify Risk of COVID-19 in Patients with Inflammatory Bowel Disease. Gastroenterology. 2020:S0016–5085(20)34738–7.
9. Allocca M, Fiorino G, Zallot C, Furfaro F, Gilardi D, Radice S, et al. Incidence and Patterns of COVID-19 Among Inflammatory Bowel Disease Patients From the Nancy and Milan Cohorts. Clinical Gastroenterology and Hepatology.
10. Derikx LAAP Lantinga MA, de Jong DJ, van Dop WA, Creemers RH, Römkens TEH, et al. Clinical Outcomes of Covid-19 in Patients With Inflammatory Bowel Disease: A Nationwide Cohort Study. Journal of Crohn's and Colitis. 2020.
11. Burke KE, Kochar B, Allegretti JR, Winter RW, Lochhead P, Khalili H, et al. Immunosuppressive Therapy and Risk of COVID-19 Infection in Patients With Inflammatory Bowel Diseases. Inflammatory Bowel Diseases. 2020.
12. Khan N, Patel D, Xie D, Lewis J, Trivedi C, Yang Y-X. Impact of Anti-TNF and Thiopurines medications on the development of COVID-19 in patients with inflammatory bowel disease: A Nationwide VA cohort study. Gastroenterology. 2020.
13. D'Amico F, Danese S, Peyrin-Biroulet L. Systematic review on IBD patients with COVID-19: it is time to take stock. Clinical Gastroenterology and Hepatology.
14. Ouali SE, Achkar J-P, Lashner B, Regueiro M. Gastrointestinal manifestations of COVID-19. Cleveland Clinic Journal of Medicine. 2020.
15. El Ouali S, Philpott J, Vargo J, Regueiro M. COVID-19 in patients with IBD and pancreaticobiliary disorders. Cleveland Clinic Journal of Medicine. 2020.
16. Taxonera C, Fisac J, Alba C. Can COVID-19 trigger de novo inflammatory bowel disease? Gastroenterology. 2020.
17. Effenberger M, Grabherr F, Mayr L, Schwaerzler J, Nairz M, Seifert M, et al. Faecal calprotectin indicates intestinal inflammation in COVID-19. Gut. 2020:gutjnl-2020–321388.
18. Brenner EJ, Ungaro RC, Colombel JF, Kappelman MD. SECURE-IBD Database Public Data Update. covidibd.org. Accessed on 02/13/21
19. Bezzio C, Saibeni S, Variola A, Allocca M, Massari A, Gerardi V, et al. Outcomes of COVID-19 in 79 patients with IBD in Italy: an IG-IBD study. Gut. 2020;69(7):1213–7. [PubMed: 32354990]
20. Brenner EJ, Ungaro RC, Gearry RB, Kaplan GG, Kissous-Hunt M, Lewis JD, 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.**This important study is the first analysis of the SECURE-IBD registry. It greatly contributed to our knowledge about the impact of IBD therapies in the setting of COVID-19.

21. D'Amico F, Danese S, Peyrin-Biroulet L. Systematic Review on Inflammatory Bowel Disease Patients With Coronavirus Disease 2019: It Is Time to Take Stock. Clinical Gastroenterology and Hepatology. 2020;18(12):2689–700. [PubMed: 32777550]
22. Ungaro RC, Brenner EJ, Gearry RB, Kaplan GG, Kissous-Hunt M, Lewis JD, et al. Effect of IBD medications on COVID-19 outcomes: results from an international registry. Gut. 2020:gutjnl-2020–322539.*This study is an expanded analysis of the SECURE-IBD registry and provides further insights on the impact of IBD therapies in the context of SARS-CoV-2 infection.
23. Dexamethasone in Hospitalized Patients with Covid-19 — Preliminary Report. New England Journal of Medicine. 2020.
24. Magro F, Dias CC, Morato M. Aminosalicylates and COVID-19: Facts or Coincidences? Gastroenterology. 2020.
25. Papa A, Gasbarrini A, Tursi A. Epidemiology and the Impact of Therapies on the Outcome of COVID-19 in Patients With Inflammatory Bowel Disease. Am J Gastroenterol. 2020.
26. Rizk JG, Kalantar-Zadeh K, Mehra MR, Lavie CJ, Rizk Y, Forthal DN. Pharmaco-Immunomodulatory Therapy in COVID-19. Drugs. 2020.
27. Dolinger MT, Person H, Smith R, Jarchin L, Pittman N, Dubinsky MC, et al. Pediatric Crohn's Disease and Multisystem Inflammatory Syndrome in Children (MIS-C) and COVID-19 Treated with Infliximab. J Pediatr Gastroenterol Nutr. 2020:10.1097/MPG.0000000000002809.
28. Bezzio C, Manes G, Bini F, Pellegrini L, Saibeni S. Infliximab for severe ulcerative colitis and subsequent SARS-CoV-2 pneumonia: a stone for two birds. Gut. 2020:gutjnl-2020–321760.
29. Lees CW, Irving PM, Beaugerie L. COVID-19 and IBD drugs: should we change anything at the moment? Gut. 2020:gutjnl-2020–323247.
30. Agrawal M, Brenner EJ, Zhang X, Modesto I, Woolcott J, Ungaro RC, et al. Characteristics and Outcomes of IBD Patients with COVID-19 on Tofacitinib Therapy in the SECURE-IBD Registry. Inflammatory Bowel Diseases. 2020.
31. Kennedy NA, Jones G-R, Lamb CA, Appleby R, Arnott I, Beattie RM, et al. British Society of Gastroenterology guidance for management of inflammatory bowel disease during the COVID-19 pandemic. Gut. 2020;69(6):984–90. [PubMed: 32303607]
32. Rubin DT, Abreu MT, Rai V, Siegel CA, International Organization for the Study of Inflammatory Bowel D. Management of Patients With Crohn's Disease and Ulcerative Colitis During the Coronavirus Disease-2019 Pandemic: Results of an International Meeting. Gastroenterology. 2020:S0016–5085(20)30465–0.**Important consensus guidance for the management of IBD during the COVID-19 pandemic.
33. Rubin DT, Feuerstein JD, Wang AY, Cohen RD. AGA Clinical Practice Update on Management of Inflammatory Bowel Disease During the COVID-19 Pandemic: Expert Commentary. Gastroenterology. 2020.
34. Dotan I, Panaccione R, Kaplan GG, O'Morain C, Lindsay JO, Abreu MT, et al. Best Practice Guidance for Adult Infusion Centres during the COVID-19 Pandemic: Report from the COVID-19 International Organization for the Study of IBD [IOIBD] Task Force. Journal of Crohn's and Colitis. 2020;14(Supplement_3):S785–S90.
35. Siegel CA, Christensen B, Kornbluth A, Rosh JR, Kappelman MD, Ungaro RC, et al. Guidance for Restarting Inflammatory Bowel Disease Therapy in Patients Who Withheld Immunosuppressant Medications During COVID-19. Journal of Crohn's and Colitis. 2020;14(Supplement_3):S769–S73.
36. Lewin S, Lees C, Regueiro M, Hart A, Mahadevan U, Diseases ftIOftSoIB. International Organization for the Study of Inflammatory Bowel Disease: Global Strategies for Telemedicine and Inflammatory Bowel Diseases. Journal of Crohn's and Colitis.2020;14(Supplement_3):S780–S4.

37. Ng SC, Mak JWY, Hitz L, Chowers Y, Bernstein CN, Silverberg MS. COVID-19 Pandemic: Which IBD Patients Need to Be Scoped-Who Gets Scoped Now, Who Can Wait, and how to Resume to Normal. J Crohns Colitis. 2020;14(Supplement_3):S791–S7. [PubMed: 33085973]
38. Magro F, Rahier J-F, Abreu C, MacMahon E, Hart A, van der Woude CJ, et al. Inflammatory Bowel Disease Management During the COVID-19 Outbreak: The Ten Do's and Don'ts from the ECCO-COVID Taskforce. Journal of Crohn's and Colitis. 2020;14(Supplement_3):S798–S806.
39. Allez M, Fleshner P, Gearry R, Lakatos PL, Rubin DT, Disease obotIOftSoIB. Care of the Patient With IBD Requiring Hospitalisation During the COVID-19 Pandemic. Journal of Crohn's and Colitis. 2020;14(Supplement_3):S774–S9.
40. Remzi FH, Panis Y, Spinelli A, Kotze PG, Mantzaris G, Söderholm JD, et al. International Organization for the Study of IBD Recommendations for Surgery in Patients With IBD During the Coronavirus Disease 2019 Pandemic. Dis Colon Rectum. 2020;63(7):870–3. [PubMed: 32355056]
41. CDC. Available from: https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/prevention.html. [Accessed 13 Feb. 2021]
42. Siegel CA, Melmed GY, McGovern DP, Rai V, Krammer F, Rubin DT, et al. SARS-CoV-2 vaccination for patients with inflammatory bowel diseases: recommendations from an international consensus meeting. Gut. 2021.* Consensus recommendations regarding COVID-19 vaccinations in patients with IBD.
43. Van Assche G, Vermeire S, Ballet V, Gabriels F, Noman M, D'Haens G, et al. Switch to adalimumab in patients with Crohn's disease controlled by maintenance infliximab: prospective randomised SWITCH trial. Gut. 2012;61(2):229–34. [PubMed: 21948942]
44. Rosen MH, Axelrad J, Hudesman D, Rubin DT, Chang S. Management of Acute Severe Ulcerative Colitis in a Pregnant Woman With COVID-19 Infection: A Case Report and Review of the Literature. Inflamm Bowel Dis. 2020;26(7):971–3. [PubMed: 32393973]
45. Baden LR, El Sahly HM, Essink B, Kotloff K, Frey S, Novak R, et al. Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine. New England Journal of Medicine. 2020.
46. Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, et al. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. New England Journal of Medicine. 2020;383(27):2603–15.
47. Knoll MD, Wonodi C. Oxford-AstraZeneca COVID-19 vaccine efficacy. The Lancet. 2020.
48. Melmed GY, Rubin DT, McGovern DPB. Winter is coming! Clinical, immunological, and practical considerations for vaccinating patients with IBD during the COVID pandemic. Gastroenterology. 2020.

Key points

- Patients with IBD are not at increased risk of SARS-CoV-2 infection overall
- Moderate to severe disease activity, obesity and corticosteroids have been associated with an increased risk of COVID-19 infection
- Although patients with IBD are not at increased risk of severe COVID-19, several factors such as older age, comorbidities, active IBD and corticosteroid use have been associated with worse COVID-19 outcomes
- Non-live COVID-19 vaccines should be offered to patients with IBD, regardless of immunosuppressant use

TABLE 1.

Risk factors for severe COVID-19 outcomes in patients with IBD

Risk factor	References
Comorbidities*	Bezzio et al. (19) Brenner et al. (20) Derikx et al. (10) D'Amico et al. (21)
Active IBD	Bezzio et al. (19)
Older age	Bezzio et al. (19) Brenner et al. (20) Burke et al. (11)
Systemic corticosteroids	Brenner et al.** (20) Ungaro et al.** (22)
Obesity	Burke et al. (11)
5-Aminosalicylates	Brenner at al.** (20) Ungaro et al.** (22)
Thiopurines***	Ungaro et al. (22)
Combination therapy (thiopurine with anti-TNF)	Ungaro et al. (22)

*Definitions of comorbidities varied among studies but generally included hypertension, diabetes, cardiovascular disease, and lung, kidney or liver disease

**These studies partially included the same patient population as part of the SECURE-IBD registry

***When compared to anti-TNF therapy

TABLE 2.

IBD management during the COVID-19 pandemic: general recommendations

Aspects of IBD care	Recommendations	Guidance
Medication management	Infusions should be continued at a center with a COVID-19 screening protocol and appropriate safety measures	– IOIBD(33) – AGA(34)
	Intravenous medications should not be switched to a different subcutaneous medication	AGA(33) IOIBD(34)
	IBD therapy should not be held except for corticosteroids which should be tapered or stopped	– IOIBD(32) – AGA(33)
	In case of SARS-CoV-2 infection, immunosuppressive therapy should generally be held for at least 10 days from symptom onset	– IOIBD(35)
Disease monitoring	Telemedicine is encouraged	– IOIBD(36, 37) – ECCO(38)
	Endoscopy: Procedures should be performed according to adequate safety measures and prioritized according to the urgency of their indication	
	Laboratory tests: Clinical evaluation combined with fecal calprotectin and serum inflammatory markers can be used as alternative monitoring tools if endoscopy is not readily available	
	The implementation of point-of-care biomarkers and home fecal calprotectin tests is encouraged	
Hospitalization	Hospitalization should only be pursued if absolutely necessary	– IOIBD(39)
	Endoscopic or radiologic procedures should only be performed if urgently required or if susceptible to change management	
	Length of stay should be minimized	
Surgery	Preoperative SARS-CoV-2 testing is required prior to surgery	– IOIBD(40) – ECCO(38)
	Surgery should be postponed in uncomplicated IBD	
Preventive care	Inactivated influenza vaccine and pneumococcal vaccine are strongly encouraged	– ECCO(38)
COVID-19 prevention	Usual preventive measures should be encouraged: social distancing, hand hygiene, using a mask, avoidance of travel and crowds	AGA(33) – ECCO(38) – CDC(41)
	Non-live COVID-19 vaccine should be recommended to all patients with IBD, regardless of immunosuppressive therapy	– IOIBD(42)

Abbreviations: AGA, American Gastroenterological Association; CDC, Centers for Disease Control and Prevention; ECCO, European Crohn's and Colitis Organisation; IOIBD, International Organization for the study of Inflammatory Bowel Disease