

**TITLE: *Care of the Patient with IBD Requiring Hospitalization During the COVID-19 Pandemic***

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## Disclosures

Matthieu Allez has received grant support from Janssen and Genentech and has been a speaker and/or advisory board member for Amgen, Biogen, Boehringer Ingelheim, Celgene, Ferring, Genentech, Janssen, Pfizer, Takeda, Tillots and Roche.

Phillip Fleshner has served as a consultant for Takeda.

Richard Garry has received honoraria, research support and has sat on scientific advisory boards for AbbVie, Janssen and Zespri.

Peter L. Lakatos has been a speaker and/or advisory board member: AbbVie, Arena Pharmaceuticals, Celltrion, Falk Pharma GmbH, Ferring, Genentech, Janssen, Merck, Pharmacosmos, Pfizer, Roche, Shire and Takeda and has received unrestricted research grant: AbbVie, MSD and Pfizer.

David T. Rubin has received grant support from Takeda and has served as a consultant for Abbvie, Abgenomics, Allergan Inc., Boehringer Ingelheim Ltd., Bristol-Myers Squibb, Celgene Corp/Syneos, Check-cap, Dizal Pharmaceuticals, GalenPharma/Atlantica, Genentech/Roche, Gilead Sciences, Ichnos Sciences S.A., GlaxoSmithKline Services, Janssen Pharmaceuticals, Lilly, Narrow River Mgmt, Pfizer, Prometheus Laboratories, Reistone, Shire, Takeda, and Techlab Inc.

## Author Contributions

The authors have made substantial contributions to all of the following: (1) the conception and design of the study, (2) drafting the article or revising it critically for important intellectual content, (3) final approval of the version to be submitted.

## Abstract

The management of IBD has been highly impacted in the context of the COVID-19 pandemic, with restriction of hospitalizations and unprecedented redeployment of healthcare resources. Hospital admissions of IBD patients should be limited to reduce the risks of coronavirus transmission. However, delaying hospitalization of IBD patients with severe or complicated disease may increase the risk of poor outcomes. Delaying surgery in some cases may increase the risk of disease progression, post-operative morbidity and disease complications. IBD patients who are infected with SARS-CoV-2 may have a higher risk of poor outcomes than the general population, potentially related to concomitant medications, especially corticosteroids. There is no evidence today that IBD patients with COVID-19 have worse outcomes if they receive immunosuppressant medications including thiopurines, biologics and novel small molecules. This article summarizes recommendations by the international membership of IOIBD regarding hospitalizations of IBD patients, either for active or complicated IBD or severe COVID-19, and for management of IBD patients according to SARS-CoV-2 infectious status.

## Introduction

The COVID-19 pandemic has led to restriction of hospitalizations and unprecedented redeployment of healthcare resources. The management of IBD has been highly impacted.<sup>1-4</sup> On the one hand, hospital admissions of IBD patients should be limited to reduce the risks of coronavirus transmission between hospitalized patients and to ensure that there is inpatient capacity to look after the many admissions with COVID-19.<sup>5</sup> On the other hand, delaying hospitalization of IBD patients with severe or complicated disease may increase the risk of poor outcomes. Surgery is also seriously impacted in the present context.<sup>6,7</sup> A number of emergencies require surgery in the short term, and delaying surgery in some cases may increase the risk of disease progression, post-operative morbidity and disease complications. Performance of endoscopic procedures is also impacted, with significant delays to routine endoscopy.<sup>8</sup> In this context, we have developed recommendations regarding hospitalizations of IBD patients, either for active or complicated IBD or severe COVID-19 disease, and for management of IBD patients according to SARS-CoV-2 infectious status. These recommendations are based on expert opinion and the limited evidence that has been published in this area. After their development the recommendations were reviewed by the membership of IOIBD. These recommendations should be read in conjunction with other IOIBD recommendations in this issue of the *Journal of Crohn's and Colitis*.

IBD patients do not appear to have an increased risk of being infected with SARS-CoV-2.<sup>2,9</sup> However, IBD patients who are infected with SARS-CoV-2 may have a higher risk of poor outcomes than the general population.<sup>10</sup> This increased risk may be driven by concomitant medications, especially corticosteroids, but may also be associated with gastrointestinal inflammation, IBD itself or associated comorbidities. Additional risk factors for poor outcomes

from COVID-19 include older age, pre-existing cardiovascular and respiratory disease, obesity, diabetes and cigarette smoking.<sup>11</sup> While the use of immunosuppressing medications such as thiopurines, and biologics has been associated with increased risks of a range of infections in IBD patients, at this point, there is no evidence that IBD patients with COVID have worse outcomes if they receive these drugs.<sup>10,12,13</sup> National and international societies, including IOIBD, have recommended the maintenance of these therapies in the present context.<sup>14</sup>

Which IBD drugs should be preferentially used to induce response or remission in patients with active IBD during the COVID-19 pandemic is unclear. There is even less evidence on how IBD patients with active disease should be treated according to their COVID-19 infectious status. Manifestations and outcomes from COVID-19 infection are related to host defense responses. The hyper-inflammatory response may lead to organ failures, associated with a cytokine “storm”, characterized by high levels of pro-inflammatory cytokines, such as TNF, several interleukins and chemokines. Immunomodulation of this hyperinflammatory state is currently being explored<sup>15</sup>, and there are several clinical trials in COVID-19 patients of immunomodulators or targeted therapies.<sup>16</sup> It is possible that even if immunomodulators suppress viral immunity, they may exert a beneficial effect by controlling the hyperinflammatory state.

COVID-19 can cause diarrhea and abdominal pain and may mimic an IBD flare.<sup>17</sup> The virus can infect the gut, as demonstrated by a positive SARS-CoV-2 viral nucleocapsid positive staining in digestive biopsies.<sup>18</sup> It is currently unknown if SARS-CoV-2 can cause relapse of or *de novo* IBD. A striking characteristic of severe COVID-19 infections is the predisposition to develop thromboembolic complications.<sup>19–23</sup> Given that IBD patients are already at risk, anticoagulation prophylaxis should be adapted to each situation.

These recommendations, based on our limited current knowledge on COVID-19, will be updated over time. They should be interpreted in the context of the prevalence of COVID-19 in your community, availability of healthcare resources including personal protection equipment, available personnel and local regulations or policies related to the pandemic.

### **Proposed statements**

#### 1. Criteria for admission

- a. Patients with severe or complicated disease or with emergencies should be evaluated and admitted as prior to the pandemic. Patients who are less active but who would under usual circumstances be admitted for medically resistant disease should not be electively admitted at this time.
- b. If available, rapid access outpatient evaluation and outpatient treatment escalation is preferable. When appropriate and available, telemedicine options should be utilized (Refer to IOIBD Telemedicine guidance document.)
- c. Patients with IBD and COVID-19 should be admitted based on considerations of the severity of the COVID-19 and the severity of the IBD.
- d. Bypassing the emergency room with direct admission to the hospital ward is preferable. However, this will depend on admission protocols in place at individual hospitals.
- e. Depending on institutional policy and availability, testing for SARS-CoV-2 may be required prior to needed inpatient endoscopic, radiologic or surgical procedures, as even asymptomatic patients with SARS-CoV-2 infection may be at risk for postoperative ICU care and mortality<sup>24,25</sup>, and are at risk for infecting others.

- f. Ideally, and when possible, testing for SARS-CoV-2 should be performed before admission. We recommend to hospitalize the patient in a single room until the result of testing for SARS-CoV-2 is available.
2. Evaluation for COVID-19
    - a. Patients suspected of having COVID-19 should be tested for SARS-CoV-19 in the nasopharynx. Serologic antibody testing may also be used, provided that this testing is both accurate and has clinical relevance. Testing for SARS-CoV-2 is evolving and it is currently unclear which test will be best.
    - b. If testing for SARS-CoV-2 is negative, or if the patient is considered as immune, the patient can be admitted to a COVID-free unit.
    - c. Patients positive for SARS-CoV-19 or suspected to have COVID-19 should be isolated in a negative pressure room, and ideally admitted to a specific unit. Healthcare workers should utilize appropriate PPE and follow local infection control guidelines.
    - d. It is unknown if SARS-CoV-2 can cause relapse of or *de novo* IBD.
    - e. Universal stool testing for SARS-CoV-2 is not recommended at this time.
  3. Diagnostic considerations
    - a. Laboratory investigations should be chosen and utilized to minimize need for interventions and to those that will directly influence medical or surgical management, with mindfulness on laboratory resource utilization.

- b. Radiologic procedures should be limited to those that are urgently needed or will directly influence management, e.g., AXR, CT or MR to evaluate for abscess or obstruction. In the current environment, CT may be preferred over MR due to faster acquisition time and easier deep cleaning of equipment.
  - c. Endoscopic procedures should be limited to those that are urgently needed or will directly influence management. Serum and stool biomarkers may have a more prominent role to play in this setting. (Refer to IOIBD Endoscopy guidance document.)
4. Considerations for treatment of IBD in a patient with SARS-CoV-2
- a. Table 1 is a summary of treatment considerations based on IBD and COVID-19 severity. This table is mainly based on expert opinion and published recommendations from professional bodies.
  - b. Choice of IBD therapies in this setting must be considered in the context of the severity of the COVID-19.
  - c. In cases of moderate-severe COVID-19, discontinuation of IBD therapies must be discussed case-by-case, according to IBD activity and treatment. Interestingly, some treatments such as steroids and even some biologics are considered and even assessed in ongoing clinical trials in the second phase of COVID-19 (so called cytokine storm).
  - d. Given the standard of practice for all hospitalized IBD patients and the emerging understanding of hypercoagulability associated with severe COVID-19, patients with COVID and active IBD require specific attention regarding anticoagulation



prophylaxis. Doses of heparin required should be in line with current recommendations, considering both IBD and COVID-19 risks.

- e. Patients with persistent hypoxia (O<sub>2</sub> saturation < 90% on NC at 6 L/min), rapid worsening of hypoxia or altered mental status require ICU management.
5. Treatment of the IBD patient hospitalized for medically resistant disease (and without COVID-19)
- a. Given the risk of COVID-19 in the community or even in the hospital, choices of therapy should be based on combination of efficacy, safety, speed of onset, and limitation of need for outpatient monitoring once discharged.
  - b. Length of stay should be minimized but should not compromise successful disease control.
  - c. In addition to standard medical therapies, EEN can be considered in patients with Crohn's disease, particularly as an alternative to systemic steroids in those with moderate disease. Close support from a dietitian is likely to improve acceptability and tolerance of this approach
6. Surgery (Refer to IOIBD Surgery guidance document.)
- a. Colectomy for severe/fulminant UC.

Although surgical societies have recommended that elective surgical cases be postponed, surgery for imminently life-threatening conditions such as medically refractory severe UC (or cancer development) should continue as clinically indicated.<sup>26</sup> This minimizes the risk

to both patient and health care team, as well as minimizes utilization of necessary resources, such as beds, ventilators, and personal protective equipment (PPE).

- b. Surgery for IBD patients with dysplasia or cancer should be delayed at the current time and rescheduled when resources are available. Delays should be minimized as much as possible within the limits of available resources. Clinicians should maintain accurate records of deferred procedures and should prioritize these patients once surgical slots become available.
- c. Treatment of perianal disease and/or perineal sepsis in CD

- i. Surgery for asymptomatic perianal fistulas should be postponed. Setons can remain in place. Seton removal alone in patients on biologic therapy should be reconsidered in order to minimize recurrent abscess formation and need for further hospitalization.
- ii. For small perianal abscesses, it is reasonable to try a short course of antibiotic therapy before surgery. However, the role of oral antibiotic therapy alone versus surgical drainage for small abscesses in these patients is unknown.
- iii. The presence of a large or complex perianal abscess in the CD patient requires surgery and should not be delayed.

- d. Surgery for CD

- i. Bowel obstruction.

- 1. Modification of nasogastric (NG) suctioning handling. As the virus has been isolated from multiple cells and body fluids including enteric contents<sup>27</sup>, placement and handling of NG tubes should be

performed by care members donning appropriate PPE, including gowns and face shields.

2. CD patients with intestinal obstruction not improving with medical therapy require surgery including stricturoplasty and/or resection with primary anastomosis.
3. The value of performing a stoma routinely in these cases, although advised by some societies to reduce need for unplanned post-operative critical care for complications<sup>24</sup>, is of uncertain benefit.

ii. Intra-abdominal abscess

1. Treat with standard approach to drainage of the abscess, bowel rest and antibiotic therapy.
2. When needed, surgery in this situation should not be delayed

7. Exclusion of visitors in the hospital during hospitalization or recovery. Most hospitals are not allowing visitors in any patient care areas, exceptions being one caregiver for patients under the age of 18. The social and emotional impact of these policies on the IBD patient requiring hospitalization or facing surgery are formidable. Efforts should be made to communicate with family and to encourage video conferencing with family and patients when possible.

In conclusion, the usual management of IBD is strongly impacted by the COVID-19 pandemic, and must be adapted over time according to the local situation and prevalence of COVID-19. The objectives of these recommendations are to reduce the risks of contamination, to provide an

optimal management of COVID-19 in IBD patients, and to best manage IBD according to SARS-CoV-2 infectious status. These recommendations, based on our limited current knowledge on COVID-19, will be updated over time according to a better knowledge of the disease.

### **Questions which should be addressed and/or resolved in the near future**

- What will be the global impact of reduced IBD hospitalizations and delayed surgery during the Covid-19 pandemic?
- How should we best organize the testing for SARS-CoV-2 in IBD patients requiring hospitalization? Is SARS-CoV-2 serology useful in this context? Is SARS-CoV-2 serology valid as well in patients receiving immunosuppressants?
- Can SARS-CoV-2 be involved in relapse of or *de novo* IBD? Are there long-term effects of Covid-19 in IBD patients?
- Are IBD patients at increased risks of Covid-19 infection? Are Covid-19 infections more severe in IBD patients?
- Are there specific risks which could be attributed to the different IBD drugs, including steroids, immunosuppressive/modulators?
- How should we best treat active IBD in the context of the Covid-19 pandemic?
- How should we best treat active IBD in patients with Covid-19 infection?
- How should be best prevent thrombosis in patients with IBD and COVID-19?

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Table: Considerations of the treatment of IBD in the setting of COVID-19

	No SARS-CoV-2	SARS-CoV-2 positive, but NO COVID-19	Mild COVID-19 Not hospitalized OR Hospitalized with SpO2 >94% and no evidence of pneumonia	Moderate COVID-19 (Hospitalized patient with hypoxia OR Radiographic evidence of pneumonia) OR Severe COVID-19 (Patient requiring mechanical ventilation +/- pressors or evidence of end organ damage)
<b>IBD remission</b>	<ul style="list-style-type: none"> <li>Taper or discontinue prednisone</li> <li>Continue all other IBD meds</li> </ul>	<ul style="list-style-type: none"> <li>If IBD stable, wait for 2 weeks for COVID-19 to present or until convalescent titers of SARS-CoV-2 develop.</li> <li>Taper or discontinue prednisone.</li> <li>Discontinue thiopurines, MTX, tofacitinib for 2 weeks.</li> <li>Delay dosing of biologics for 2 weeks.</li> </ul>	<ul style="list-style-type: none"> <li>Taper or discontinue prednisone.</li> <li>Discontinue thiopurines, MTX, tofacitinib.</li> <li>Discontinue biological therapies.</li> <li>Restart IBD therapy when COVID-19 resolved (symptoms and when validated, serological testing of convalescent titers of SARS-CoV-2 immunity).</li> </ul>	<ul style="list-style-type: none"> <li>Taper or discontinue prednisone.</li> <li>Discontinue immune based IBD therapies.</li> <li>Focus on life support and if available, treatment of COVID-19 with antiviral or other anti-inflammatory/anti-cytokine therapies.</li> <li>Prophylaxis against VTE for COVID-19</li> </ul>
<b>IBD mildly active</b>	<ul style="list-style-type: none"> <li>Treat with any IBD therapies necessary.</li> <li>Limit use of oral or IV steroids to shortest time possible, choose alternatives when possible.</li> </ul>	<ul style="list-style-type: none"> <li>If IBD stable, wait for 2 weeks for COVID-19 to present or until convalescent titers of SARS-CoV-2 develop.</li> <li>If treatment needed, budesonide, 5-ASA, rectal therapies ok.</li> <li>Consider holding immune therapies and biologics for 2 weeks.</li> </ul>	<ul style="list-style-type: none"> <li>If IBD stable, wait for 2 weeks for COVID-19 symptoms to resolve or until convalescent titers of SARS-CoV-2 develop.</li> <li>If treatment needed, budesonide, 5-ASA, rectal therapies ok.</li> <li>Taper or discontinue prednisone.</li> <li>Discontinue thiopurines, MTX, tofacitinib for 2 weeks.</li> <li>Delay dosing of biologics for 2 weeks.</li> </ul>	<ul style="list-style-type: none"> <li>Taper or discontinue prednisone.</li> <li>Discontinue immune based IBD therapies.</li> <li>Focus on life support and if available, treatment of COVID-19 with antiviral or other anti-inflammatory/anti-cytokine therapies.</li> <li>Prophylaxis against VTE for IBD and for COVID-19</li> </ul>
<b>IBD moderately - severely active</b>	<ul style="list-style-type: none"> <li>Treat with any IBD therapies necessary.</li> <li>Limit use of oral or IV steroids to shortest time possible, choose alternatives when possible.</li> <li>Prophylaxis against VTE (if hospitalized)</li> </ul>	<ul style="list-style-type: none"> <li>Limited use of corticosteroids ≤40 mg/d if necessary.</li> <li>Avoid thiopurines, MTX, tofacitinib.</li> <li>Escalate to biological therapies as needed.</li> <li>If hospitalized, consider IV cyclosporine for UC given limited evidence of benefit against coronavirus.</li> <li>Prophylaxis against VTE For IBD.</li> </ul>	<ul style="list-style-type: none"> <li>Limited use of steroids ≤40 mg/d if necessary.</li> <li>Avoid thiopurines, MTX, tofacitinib.</li> <li>Escalate to biological therapies as needed.</li> <li>Prophylaxis against VTE for IBD</li> </ul>	<ul style="list-style-type: none"> <li>Limited use of IV steroids for IBD only if necessary.</li> <li>Topical (rectal) therapy if needed.</li> <li>Discontinue immune therapies or biologics that are not working for the IBD.</li> <li>Prophylaxis against VTE for IBD and for COVID-19</li> <li>Careful consideration of other therapies for IBD only as absolutely needed. Consider cyclosporine for UC given limited evidence of benefit against coronavirus.</li> <li>Focus on life support and if available, treatment of COVID-19 with antiviral or other anti-inflammatory/anti-cytokine therapies.</li> </ul>