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## Severe Inflammatory Bowel Disease Flares and COVID-19: Expand the Gastroenterology–Surgery Team to Include an Infectious Disease Specialist



Dear Editors:

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a new virus that was first identified in Wuhan, China, and has now spread worldwide. It causes a potentially fatal infectious respiratory syndrome called coronavirus disease 2019 (COVID-19), which has rapidly evolved into a pandemic.<sup>1</sup> COVID-19 is a major health emergency that has had a substantial impact on everyday clinical practice. It has raised several new questions and concerns about its potential impact on patients with chronic illnesses, especially those treated with immunomodulating drugs.

In the field of inflammatory bowel disease (IBD), the British Society of Gastroenterology<sup>2</sup> and American Gastroenterological Association<sup>3</sup> have recently provided guidance on the management of patients with Crohn's disease and ulcerative colitis during this complicated period. For example, the American Gastroenterological Association recommends following standard therapeutic algorithms for patients hospitalized for IBD who also have mild or incidentally identified COVID-19.<sup>3</sup> It also recommends scheduling the usual surgical consultation, but acknowledges that it is reasonable to medically attempt to postpone surgery during the pandemic. Perhaps because of the lack of empirical evidence, these guidelines did not specifically address the challenging case of IBD patients hospitalized owing to a severe flare of disease with subsequent or concomitant pneumonia owing to SARS-CoV-2.

Especially in ulcerative colitis, a severe flare of disease is a life-threatening emergency that requires prompt recognition, hospitalization, early initiation of treatment, and close monitoring.<sup>4</sup> The outcome of severe flares is measured in terms of surgery and mortality rates. Therefore, a multidisciplinary approach involving a gastroenterologist and a colorectal surgeon is essential. This professional pair shares the responsibility in correctly identifying the most effective type and timing of rescue therapy or surgery. However, in the COVID-19 pandemic, this professional pair may not be enough to effectively manage the infection in an IBD patient with a severe disease flare.

We recently published a prospective, observational study of 79 IBD patients with COVID-19.<sup>5</sup> The study found that active disease, age >65 years and comorbidities associated with worse outcomes, both pneumonia and death,

whereas the use of immunosuppressant and biological therapies did not. Four of the patients had been diagnosed with the infection during hospitalization for a severe flare of IBD, and 2 of them died. To further illustrate the therapeutic challenge these patients present, here we examine the emblematic new case of a 40-year-old man who was admitted to our hospital for severe clinical and endoscopic recurrence of ulcerative pancolitis not responding to systemic oral steroids. At admission, he reported bloody diarrhea, with >15 bowel movements per day, and mild abdominal pain. Laboratory tests showed mild normocytic anemia and markedly increased C-reactive protein. Chest and abdominal radiographs were normal, and a nasopharyngeal swab for SARS-CoV-2 was negative. After 6 days of intravenous steroids with an unsatisfactory clinical response, excluded colonic superinfection with cytomegalovirus, we began to consider the need for salvage therapy with infliximab. However, the same day, the patient developed fever (38.5°C) and cough, and repeat chest radiography demonstrated interstitial pneumonia. A new nasopharyngeal swab was positive for SARS-CoV-2. Therefore, intravenous steroids were tapered, and azithromycin and hydroxychloroquine were started according to local protocols.

At this point, the gastroenterologist and surgeon involved an infectious disease specialist in determining the best therapeutic strategy among several options: (1) surgery, (2) a drastic decrease in of steroids and starting with cyclosporine, and (3) a drastic decrease in steroids and starting with infliximab. Option 1 offered the possibility of fully solving the gastrointestinal problem, but poses a risk of fatal complications in patients with COVID-19.<sup>6</sup> Options 2 and 3 offered a likely clinical response of the gastrointestinal disease<sup>4</sup> and a potential therapeutic effect on the infection,<sup>7,8</sup> but could also worsen the course of infection and complicate a later surgical intervention. Finally, assessing the risk–benefit ratio we decided to start with infliximab at 5 mg/kg.

We do not yet know what will be the final effect of this treatment and the outcome for the patient. Nonetheless, we think that the issues raised by this case are of great interest to physicians managing IBD patients during the COVID-19 pandemic. In particular, we suggest that an infectious disease specialist join the gastroenterologist and surgeon on the team managing IBD patients hospitalized for a severe flare of disease. In this way, they will become “three of a perfect pair”

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## Should Patients With Inflammatory Bowel Disease Be Tested for Active COVID-19 Before Starting a Biological Treatment?



Dear Editors:

We read with great interest the review article by Rubin et al<sup>1</sup> aimed to provide recommendations regarding the management of patients with inflammatory bowel disease (IBD) in the era of the coronavirus disease 2019 (COVID-19) pandemic.<sup>1</sup> Given the rapid widespread of this infection from China to many countries in the world and our current knowledge about severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), these suggestions regarding patients with important comorbidity, such as immune-mediated diseases, and thus with poorer clinical outcome, are surely very welcome.

In particular, although available data do not support an increased risk of contracting COVID-19 infection in patients with IBD, the international Surveillance Epidemiology of Coronavirus Under Research Exclusion IBD registry reports a not reassuring 4% case fatality rate and hospitalization in nearly one-third of patients.<sup>2</sup> Moreover, a recent report from Italy showed a case fatality rate of 8% and a hospitalization rate of 28% among 79 patients with IBD with confirmed COVID-19 followed at 24 IBD referral units.<sup>3</sup>

We appreciate the recommendations by Rubin et al, especially their clarity and practical suggestions. Medication, in particular, is a priority area and the COVID-19 pandemic has led to challenging decision-making about treatment in patients with IBD. The American Gastroenterological Association suggests that patients with IBD should not stop their current treatments to prevent infection or adverse outcome with COVID-19.<sup>1</sup> Considerations on specific drugs were also provided, although robust evidence on the impact of different immunosuppressive or immunomodulatory medications on the COVID-19 related risk is still lacking. However, there was no specific international guidance with respect to COVID-19 testing in patients starting

immunosuppressive treatment, particularly if they are asymptomatic, and the article by Rubin et al did not cover this topic either.

Should an asymptomatic patient be tested for SARS-CoV-2 before undergoing the induction regimen of a biologic drug?<sup>4,5</sup> Higher concentrations of biologics are necessary for induction versus maintenance, and induction dosing has been selected to minimize immunogenicity and provide serum levels higher than in maintenance. At this time the potential benefits of testing prior starting a biologic drug are not established, but there is plausible benefit to testing based on the following observations: (1) SARS-CoV-2 infection may be asymptomatic or minimally symptomatic; (2) the potential progression to severe disease of an asymptomatic infection in the setting of intensive immunosuppression; and (3) according to disease severity, the opportunity to delay biologic treatment to allow resolution of SARS-CoV-2 infection. Another important aspect to consider is the contribution of steroids, usually adopted concomitantly with infliximab during induction or as bridge therapy, to the risk of a negative outcome in patients with COVID-19 active infection, as recently demonstrated by Lukin et al,<sup>6</sup> who showed that baseline disease activity and steroid therapy are the only variables able to stratify the risk of COVID-19 in patients with IBD.

Overall, we believe that screening for active COVID-19 infection should be performed to avoid potential complications and to adjust therapy accordingly prior starting biological treatment. Current recommendations for infection screening should be updated, at least temporarily, and testing for SARS-CoV-2 by oropharyngeal swab be included.

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