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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 al¹ 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.¹ 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 immunemediated 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.² 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.³

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-19.¹ 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?^{4,5} 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,⁶ 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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Reply. We would like to thank the colleagues who have submitted correspondences in response to our clinical practice update, "Update on Management of Inflammatory Bowel Disease During the COVID-19 Pandemic"¹ and take this opportunity to reply to their inquiries.

Professors Barberio, Buda, and Savarino raise the important question as to whether patients with inflammatory bowel disease (IBD) should be tested for coronavirus disease 2019 (COVID-19) before starting a biological therapy, especially because the induction dosing used in most instances is a higher dose and /or regimen than that used for maintenance of disease control. Although we agree that there may be patients with asymptomatic severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections among patients with moderately to severely active ulcerative colitis or Crohn's disease (the target group for biological therapy), the robust data that have emerged linking systemic corticosteroids to poor patient outcomes in COVID-19,^{2,3} along with the realization that, in the absence of biologics, systemic corticosteroids have traditionally been the "go-to drugs" support a general approach of not delaying these nonsteroid therapies. Our position was reiterated by the International Organization for the Study of Inflammatory Bowel Diseases.⁴ The American Gastroenterological Association's excellent guidelines on the topic of community based asymptomatic screening for SARS-CoV-2 infection,⁵ as well as other critical analyses of testing in the absence of a known exposure raise additional concerns about rates of false-positive and -negative results, and their implications.⁶

In a second correspondence, our Italian colleagues Bezzio and Saibeni relate a case of a patient with severely active IBD who, despite initially testing negative for SARS-CoV-2 upon admission to the hospital, subsequently received intensive corticosteroid therapy and developed symptoms that were consistent with active COVID-19 (supported by a second SARS-CoV-2 test that was positive). They adeptly point out that these patients often need a multidisciplinary approach to their IBD care, with expert input from the gastroenterologists, surgeons, and infectious disease specialists to ensure an optimal outcome. We agree, and emphasize that this case report further supports for our contention to avoid delays in initiating nonsteroid therapies in patients with moderately to severely active IBD.

The final correspondence from Drs Mago, Vaziri, and Tadros highlights the dilemma of detecting active IBD in the setting of a patient with Crohn's disease or ulcerative colitis who may be infected with the SARS-CoV-2; both conditions may result in an elevation in fecal calprotectin and, owing to the identification of SARS-CoV-2 in the stool of infected individuals,⁷ routine sigmoidoscopy or colonoscopy may unnecessarily expose the medical staff to the coronavirus.⁵ We agree with the suggestion that obtaining a fecal calprotectin

may be helpful in that a normal or mildly elevated level (the authors suggest that a threshold level of $<100 \ \mu g/g$ would be a reasonable limit)⁸ would suggest that the patient does not have active IBD and, therefore, obviate the need for urgent endoscopic evaluation.

Obviously, our experience with COVID-19 in the IBD population is evolving, and so should our clinical management strategies.⁹ We appreciate these contributions from our global colleagues.

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Conflicts of interest

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Drug-induced Acute Pancreatitis: Anecdotal Evidence vs Prospective Evaluation



Dear Editors:

We have read with great interest the analysis by Meczker et al¹ reporting on 1060 patients with drug-induced acute pancreatitis (DIAP). The authors meticulously collected data from worldwide published case reports and case series of DIAP