

The Impact of SARS-CoV-2 on Inflammatory Bowel Disease

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Keywords

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O Impacto do Vírus SARS-CoV-2 na Doença Inflamatória Intestinal

Palavras Chave

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Inflammatory bowel disease (IBD), comprising Crohn's disease and ulcerative colitis, are estimated to affect up to 0.5% of the Western World population [1]. These diseases, characterized by periods of remission and relapse, are triggered by an inappropriate chronic immune response and, consequently, the therapeutic arsenal includes a wide range of immunosuppressive medications [2].

In December 2019, the world's eyes turned to Wuhan, China, the hometown of a novel coronavirus (SARS-CoV-2), which was soon identified as the causative agent

of an emergent respiratory illness entitled the “2019 coronavirus disease” (COVID-19) [3]. The number of COVID-19 cases mushroomed quickly, posing a global public health emergency [4]. At the time of this writing, this pandemic affected more than 2.2 million people worldwide, accounting for over 145,000 deaths, numbers that continue to rise sharply [5]. Notwithstanding, in spite of the high transmission capacity, more than 80% of the patients have mild disease [6]. The risk factors for more severe illness are older age and underlying comorbidities, including diabetes, lung disease, and cardiovascular disease [7]. COVID-19 mortality is approximately 3.4%, in comparison to 1.1% for influenza, 9.6% for severe acute respiratory syndrome (SARS), and 34.4% for the Middle East respiratory syndrome (MERS) [8]. Nonetheless, it is important to take into account that severe and fatal cases may be overrepresented as milder and asymptomatic cases are likely underreported [6].

Worldwide, scientists urged to elucidate SARS-CoV-2 mechanisms in an attempt to recycle or develop the drug armamentarium. As reported for the SARS coronavirus, identified in February 2003, SARS-CoV-2 engages angiotensin-converting enzyme 2 (ACE-2) as the entry receptor [4, 9]. This receptor is expressed at higher levels in

alveolar lung cells but also in the esophageal epithelium and in absorptive enterocytes from ileum and colon [10]. Indeed, the ACE-2 receptor was reported to be important for intestinal homeostasis, and its disruption may lead to diarrhea – whose prevalence in COVID-19 patients is up to 30% [11]. Besides this, SARS-CoV-2 was identified in stomach, duodenal, and rectal biopsies, and in the stool samples of infected patients – where it may persist after it is no longer detected in sputum [12]. Together, these findings highlighted the possible fecal-oral transmission. However, whether the virus in stool remains infectious and whether this route is clinically relevant remains unknown. Similarly, currently, there is no evidence supporting that SARS-CoV-2 infection is a cause of IBD flares. Even so, as some COVID-19 manifestations may mimic an IBD exacerbation, it is advised to test patients for SARS-CoV-2 before assuming the flare diagnosis.

Immunosuppressed patients, a category into which IBD patients fit, often present atypical presentations of viral diseases. However, the impact of immunosuppression on the susceptibility to COVID-19 is still unclear. Data reported thus far did not identify immunomodulator use as a risk factor for disease severity [7, 13], even though a decreased host immune surveillance could theoretically increase virus burden. Also, groups with relative immunosuppression, like pregnant women and HIV patients, do not appear to be more prone to complications [14]. Likewise, having Crohn's disease or ulcerative colitis does not increase the risk of becoming infected with SARS-CoV-2 or developing COVID-19 [3]; to date, 526 IBD patients were reported to be infected [15]. On the other hand, considering that systemic hyperinflammation may be a driver of COVID-19 severity, it could be hypothesized that patients under immunosuppressive treatment could have milder disease [16].

In this context, there is no evidence supporting the prophylactic suspension or dose adjustment of immunosuppressive or biologic medication in patients without SARS-CoV-2, as recommended by the European Crohn's and Colitis Organization [17] and the International Organization for the study of IBD [3]. Therefore, priority must be given the achievement and maintenance of IBD remission, and patients should continue drug infusions, as the risk of flares outweighs the probability of contracting coronavirus. Two cautious exceptions are: (i) patients under high-dose steroids (>20 mg/day), where tapering must be as quickly as possible (~10 mg/week), or (ii) patients receiving combination therapy with biologics and immunomodulators, where the decision to reduce the immunosuppressor dose must be based on a case-by-case

basis [3, 18]. Notwithstanding, as it happens for all medical conditions, IBD management faces unprecedented challenges. In order to avoid any potential loss of follow-up, virtual clinical appointments must be conducted whenever possible, yet routine blood assessments may be deferred [13].

Different managements are advised in 2 different contexts: (i) when the IBD patient tested positive for SARS-CoV-2 but is still asymptomatic; and (ii) when the patient has SARS-CoV-2 and develops COVID-19. In both cases, aminosalicylate therapy may be continued [3, 17, 18]. It is still uncertain whether budesonide, antitumor necrosis factor, vedolizumab, or ustekinumab should be stopped in asymptomatic patients, yet evidence suggests that in COVID-19 patients the 2 latter biologics should be suspended. On the other hand, thiopurines (azathioprine or 6-mercaptopurine), methotrexate, and tofacitinib must be suspended in patients infected with SARS-CoV-2 regardless of the presence of symptoms [3].

In case a patient stopped IBD medication, because he had tested positive for SARS-CoV-2 or had developed COVID-19, the timing for treatment restart is not consensual. Some experts advise that treatment must be resumed after symptoms have completely vanished, or after 2 weeks in patients who kept asymptomatic [3]. On the other hand, others recommend that in COVID-19 patients drugs can just be restarted after 2 negative polymerase chain reaction tests [18].

In addition, considering the possibility of a fecal-oral route, the fact that SARS-CoV-2 may be transmittable by surfaces or objects and that aerosolization during invasive procedures may promote spread through the airborne route [19], all elective endoscopies and surgeries must be postponed. In case of emergent procedures, it is advisable, when possible, to test patients for SARS-CoV-2 [13]. Besides this, whenever a respiratory infection is suspected, procedures must be performed in a negative pressure room, with a 30-min interval among one patient's exit and the entrance of the next [19]. Surely, this recommendation is not applicable in many settings. In this regard, others suggested that after an endoscopy, windows should be opened and at least 1 h should pass before admitting the next patient [20].

In conclusion, in the current health, social, and political context, it is imperious to temporarily redefine the standards of care and to restrict the number of patients attending the hospital, prioritizing telemedicine. In spite of that, IBD patients with flares or those coming for infusions or drug collection are advised to go to their IBD center.

Disclosure Statement

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Author Contributions

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