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Conflicts of interest

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Reply. We appreciate the positive response from Dr Carlos Taxonera and colleagues[1] regarding our epidemiological study on rates of Coronavirus Disease 2019 (COVID-19) among patients with inflammatory bowel disease (IBD).[2] Our results, based on our experience in Northern California during the early days of the COVID-19 pandemic (March 4, 2020, to April 14, 2020), suggested that the prevalence of COVID-19 among patients with IBD was comparable with the general population.[2] Since our study, much data have rapidly accumulated to overcome sample size limitations and enabled us to expand and refine our understanding of the risks of COVID-19 among patients with IBD both at the national level and on a global scale.

In a retrospective, multicenter research network study (data collected from January 20, 2020, and May 26, 2020) in the United States involving more than 40 million patients from multiple health care organizations, Singh et al[3] reported COVID-19 in 232 patients with IBD and 19,776 patients without IBD. In unadjusted analysis, there was no difference in the risk of severe COVID-19 between the IBD and non-IBD groups (risk ratio [RR], 1.15; 95% CI, 0.92–1.45; $P = .23$). After propensity score matching, the risk of severe COVID-19 was similar (RR 0.93; 95% CI, 0.68–1.27; $P = .66$) between both groups.[3] In the same study, immune-mediated therapy in the preceding year was not associated with a higher risk of severe COVID-19 compared with patients with IBD not on immune-mediated therapy. However, preceding corticosteroid use was associated with an increased risk of severe COVID-19 compared with patients with IBD without corticosteroids.

In a systematic review (up to July 29, 2020) and meta-analysis of 23 studies including 243,760 patients with IBD, D'Amico et al[4] reported COVID-19 in 1028 patients with IBD (49.5% with Crohn's disease, 41.6% with ulcerative colitis) resulting in a cumulative prevalence of 0.4%. Increasing age and the presence of comorbidities were recognized as risk factors for COVID-19 and negative clinical outcomes. In another systematic review and meta-analysis (December 2019 to July 2020) by Singh et al[5] including 24 studies (patient cohorts from the United States, Spain, Iran, Italy, France, Germany, Greece, China, South Korea, Hong Kong, Taiwan, and the international registry SECURE-IBD), the pooled incidence rate of COVID-19 in patients with IBD was 4.02 (95% CI, 1.44–11.17; $I^2 = 98\%$) per 1000, whereas the pooled rate of COVID-19 in the general population was 6.59 (95% CI, 3.25–13.35; $I^2 = 100\%$) per 1000. The pooled relative risk of COVID-19 in patients with IBD was not different from the general population (relative risk 0.47; 95% CI, 0.18–1.26; $I^2 = 89$).

We agree with Taxonera et al[1] that the impact of IBD therapies on risks of COVID-19 infection acquisition and progression warrants further investigation, as immunosuppressive drugs have been linked with risk of infection in IBD.[6] In the meta-analysis by Singh et al,[5] only 5-aminosalicylic acid (5-ASA) use was associated with increased risk of COVID-19 (relative risk 1.89; 95% CI, 1.23–2.93; $I^2 = 37\%$). Furthermore, 5-ASA and steroid use were associated with increased risk of COVID-19 inpatient hospitalizations, intensive care unit admissions, and mortality, whereas there were no significant associations with immunomodulators and biologic therapies.[5] In an analysis of the SECURE-IBD registry (1439 cases from 47 countries), Ungaro et al[7] demonstrated that mesalamine (5-ASA) use was associated with severe COVID-19 compared with no 5-ASA use or anti–tumor necrosis factor monotherapy as reference groups. The authors also demonstrated that thiopurine monotherapy and the combination thiopurines with anti–tumor necrosis factor agents were associated with significantly increased risk of severe COVID-19.[6] Further studies will be needed to understand the mechanisms of how 5-ASA and steroids may confer risk of COVID-19 infection and how thiopurines may modulate COVID-19 severity in patients with IBD. Although biologic therapies have not been linked to COVID-19 susceptibility and severity in IBD, a recent study demonstrated that patients with immune-mediated inflammatory diseases receiving cytokine inhibitors have low prevalence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) seroconversion.[8] Future studies investigating the ability of patients with IBD on immunosuppressive drugs to develop robust, longstanding immunity against SARS-COV-2 after natural infection or vaccination are warranted.

In conclusion, cumulative evidence to date support our original finding that the risk of COVID-19 in patients with IBD is comparable with the general population.[2] Future shift in focus toward understanding the incidence of protective SARS-CoV-2 antibodies in patients with IBD on different therapies in light of the increasing number of patients recovering from COVID-19 and the expanding availability of COVID-19 vaccines would be highly valuable.

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The Adherence to Infusible Biologic Therapies in Inflammatory Bowel Disease Patients during the COVID-19 Pandemic: Is It Really a Problem?

Dear Editors:

We read with great interest the nationwide retrospective study by Khan et al[1] evaluating the adherence to infusible biologic therapies, defined as receiving an infusion within 10 weeks of the prior infusion, in patients with inflammatory bowel disease (IBD) during the current coronavirus disease 2019 (COVID-19) pandemic. The authors compared the adherence to infusion therapy between a cohort of patients with IBD who received infusible biologic therapies during COVID-19 and another cohort of patients with IBD who underwent the same therapies in 2019. They found that the adherence decreased from 84.6% in 2019 to 73.6% during the 2020 CoVID-19 crisis, thus recording a decrease in the weekly number of infusions in their center since late March 2020. Finally, this exploratory analysis also confirmed a significant association between nonadherence to biologics infusion and the subsequent risk of corticosteroid requirement.

To evaluate the impact of COVID-19 and the following lockdown on the routine activities of our gastroenterology unit, we collected data from all accesses for infusible biologic therapies to our infusion center between the January 8 and February 7 (before the lockdown) and between March 8 and April 7 (after the lockdown and CoVID-19 breakout).[2] In contrast with Khan et al, we did not observe a particular reduction of activity compared with the prelockdown period (280 vs 263) and at the same time we did not observe an increase of corticosteroid need or hospitalization among our patients with IBD. [2]

Surely, this pandemic with the extraordinary measures to contain the viral spread captured the public attention and generated misconceptions and fears.[3] To that end, a recent survey, conducted on a German cohort of 715 patients with IBD to investigate their perception of the emergency and their medication compliance, demonstrated that the fear was more pronounced in patients taking immunosuppressants. In particular, they were concerned about interactions between medication and COVID-19.[4] Nevertheless, 96.4% of patients adhered to their medication schedule.[4] Therefore, the rapid countermeasures adopted at many IBD centers, including ours, such as the implementation of telemedicine and distance education allowed to reassure patients with IBD about the lack of risk related to COVID-19 infection.[4,5] For instance, at our center, 1 week before the infusion, patients were contacted by email to reassure them about the lack of risk in coming to the hospital and the benefit of continuing medical therapy. Moreover, the day before the infusion each patient was contacted by phone to confirm the appointment and to explain the measures adopted to decrease the risks for all patients entering the hospital (ie, triaging for potential COVID infection). Finally, a mobile phone number was provided to the patients in case of doubts or concerns. These experiences teach us that more contact and dialogue with patients with IBD is important to reassure them and also to provide the correct information and psychological support. We should explain to our patients with chronic diseases why it is important that they adhere to therapies which are relative safe and manageable despite the COVID-19 pandemic.[6]

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