

Challenges in the Care of IBD Patients During the CoViD-19 Pandemic: Report From a “Red Zone” Area in Northern Italy

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INTRODUCTION

In December 2019, the first, troublesome news concerning a novel and highly infective viral pneumonia spreading from Wuhan (China) came to our attention.¹ It was difficult at that time to predict, let alone imagine, the magnitude of how severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) would change the way we practice medicine (not to mention our lives) only 2 months later. The first report on February 20 of a severe case of coronavirus disease 19 (CoViD-19) in a fit, young male from Codogno, a town just south of Milan, was rapidly followed by the identification of clusters of infected patients in the densely populated Lombardia region (approximately 10 million inhabitants with a density of 421.6 inhabitants/sq km) and in nearby regions within Northern Italy.²

Our hospital, Policlinico San Donato Research Hospital, is a university hospital located in the southeastern part of the Milan metropolitan area, where it represents one of the largest clinics in the territory. Our daily activity as gastroenterologists was immediately affected. We promptly implemented a strategy of phone call screenings before any gastrointestinal (GI) consults or endoscopic procedures, questioning patients about their geographic provenance (prohibiting patients from coming from the so-called red zone, the area surrounding Codogno), suspicious symptoms, and high-risk contacts. We had just started to contemplate how to safely continue our endoscopic activities in the absence of clear indications regarding the use of personal protective equipment (PPE) when within a few days the regional health system was overwhelmed by a massive number of CoViD-19 patients. Lombardia rapidly became one of the most severely affected regions of the world, with 54,802 infected individuals, identified by performing 176,953 nasopharyngeal swabs, and 10,022 deaths by April 9.³ On March 8, the entire region was declared a red zone, and 2 days later a complete national lockdown was declared.

Within the entire national territory, all nonurgent consults and procedures were cancelled and indefinitely postponed. With routine activities halted, all gastroenterologists from our GI unit except one have been reassigned to provide care to CoViD-19 patients. One after another, seven CoViD-19 units were created and staffed with doctors of various specialties to manage >200 dedicated hospital beds. A small internal medicine ward, dedicated to care for the few noninfected patients accessing the hospital for urgent medical conditions, was preserved and also used for GI emergencies. In 2 weeks our hospital, like many others in Northern Italy, was almost completely converted into a CoViD-19 hospital. Every possible effort was made to quickly increase the capacity of intensive care units (ICUs) to accommodate the alarming numbers of very sick CoViD-19 patients, including constructing new units in unused areas of the hospital or converting surgical rooms into ICUs.

These drastic measures were implemented in a very short period of time, and although necessary to counteract the devastation brought about by the outbreak, they also posed tremendous challenges to the care of patients with GI conditions, including those with inflammatory bowel diseases (IBD). Indeed, with severely reduced resources in regard to personnel, equipment, and space to manage patients, our IBD center had to face several critical issues.

COUNSELING OF PATIENTS WITH IBD

As a tertiary care center for IBD patients and one of the most prominent in the Milan metropolitan area, our IBD center from the very beginning of the CoViD-19 pandemic has been hit with a daily onslaught of phone calls and e-mails from our patients with concerns as to how the situation may affect them. Many were anxious about the necessity to postpone their already planned consults or endoscopies, and others were truly terrified of the idea of coming to the hospital for scheduled infusions or visits. Most of the questions, however, were related to patients' risk of infection, especially while on immunosuppressive therapies.

Indeed, to date, available evidence-based information regarding the risk of CoViD-19 infection in IBD is scarce. Anecdotally, IBD patients do not appear to be at higher risk of developing CoViD-19 compared with the general population. In fact, the Chinese Elite IBD Union did not identify any

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SARS-CoV-2 infected patients in their patient registry,⁴ and to date only a few infected IBD patients have been reported in the literature. Nonetheless, although these data are quite encouraging, solid epidemiologic evidence from areas with high IBD prevalence, such as in Western countries, is lacking at the present time and it is unclear whether the observations in China can be extrapolated to the rest of the IBD patient population worldwide. As such, although it is reasonable to reassure patients, this does not mean that they can ignore general precautions. Indeed, the single most important intervention we can engage in to protect our patients with IBD is to emphasize the importance of “primary prevention”: that is, avoiding, as much as possible, the risk of getting infected. This is especially true in frail patients—specifically, elderly or malnourished patients, those with several comorbidities, and those with long-standing aggressive disease—who respond poorly to current treatments. These particular IBD patients, with the aforementioned conditions, are highly likely to be at significant increased risk of severe SARS-CoV-2 infections.

The importance of hand-washing and other simple measures, such as avoiding touching the nose, ears, and eyes with dirty hands and covering the mouth and nose with a bent elbow when coughing or sneezing, is often underestimated. The possibility of orofecal transmission, suggested by the findings of viral RNA in stool even after patients have tested negative by nasopharyngeal swab,⁵ has to be considered. Routine use of PPE is still a matter of debate. Although not currently recommended by the World Health Organization because of the lack of evidence,⁶ the use of masks, even in the absence of symptoms, appears reasonable to us. In any case, the use of PPE (eg, masks and gloves) has rapidly and widely become commonplace among the general population. From this perspective, our role is also to inform patients how to correctly use these PPE devices, because incorrect behavior may paradoxically increase the risk of infection: for example, by touching the outer side of the mask, reusing the same mask for several days, touching the face with gloves, and removing gloves improperly. In addition, the need to comply with social distancing recommendations, avoiding crowded places, and not leaving home unless necessary must be stressed as much as possible. It is important to explain that coming to hospitals for nonurgent procedures or consultations is an unnecessary risk that should be absolutely avoided.

As a matter of fact, while reducing access to hospitals, we have had to rely as much as possible on telemedicine. Likely similar to most centers in Italy, our center does not use any specific system or dedicated equipment for this purpose. We have tried to do our best to provide adequate service for our IBD patients, despite the marked reduction of dedicated GI personnel, now largely reassigned to CoViD-19 units. We have managed to have at least one person (GI- or IBD-dedicated nurse) available 24/7 to answer e-mails and phone calls. This more “passive” approach may be adequate for patients with mild, stable

disease. However, for patients on biologic therapies, we have implemented a mandatory phone call-in the day before any planned hospital visit to screen for possible CoViD-19 symptoms or contact with infected individuals and to reassure patients that all possible precautions are being taken by the IBD center to reduce the risk of infection. Clinical conditions of patients on subcutaneous biologics can usually be checked by phone call; in addition, whenever possible, we use drug delivery services, established by the National Health System, specifically to provide hospital-dispensed medications to patients during this pandemic.

Of course, in centers with greater numbers of available and dedicated personnel, an “active” approach, which means reaching out to every patient with IBD to provide instructions and reassurance, should be preferred. From this point of view, specialized personnel, such as IBD-dedicated nurses, are of paramount importance.

MANAGEMENT OF IMMUNOSUPPRESSIVE THERAPIES (BIOLOGICS, THIOPURINES, STEROIDS)

Despite the fact that data from the SARS and Middle East respiratory syndrome coronaviruses did not show a higher risk in immunosuppressed patients,⁷ the impact of immunosuppressive therapies on CoViD-19 is largely unknown, and no evidence-based recommendations can be provided at this time. With only a few cases of infected IBD patients reported, this situation is particularly true in our field. Interestingly, however, immunosuppressive drugs such as hydroxychloroquine⁸ and tocilizumab⁹ have been proposed as therapies for CoViD-19. Thus, it is possible that targeting the immune system with specific compounds will reduce the immune-related lung damage characteristic of SARS-CoV-2 infection and dampen the severity of the disease. On the other hand, immunosuppressive drugs are usually associated with more severe viral infections because they may increase viral load.

Undeniably, whereas nonurgent consults and procedures in IBD patients with mild disease can safely be postponed, those on biologics are at risk of disease relapse if therapies are suddenly stopped. Accordingly, the International Organization for the Study of Inflammatory Bowel Disease¹⁰ recommends not stopping biologic therapies, including infusion therapies administered in hospitals, assuming that the infusion center provides an adequate screening protocol. We agree that in these patients the risk of causing a disease relapse when interrupting biologic therapies is probably higher than the risk of developing severe CoViD-19 because of the effects of immunomodulation; however, every effort should be made to protect them from the risk of infection. In hospitals where CoViD-19 patients are treated (like ours), the delineation of well-defined “clean” pathways is pivotal to minimize the risks of infection for non-CoViD-19 patients. If possible,

medical and nonmedical personnel involved at the infusion center should be excluded from the care of CoViD-19 patients. Counseling by phone, as addressed before, is of great importance to improve and secure adherence.

For patients being treated using thiopurines, suspension of therapy is not recommended, even though these therapies have a prolonged effect after their suspension. Combination therapy with biologics may be a situation of particular concern, but again there are currently no data available to support the suspension of one agent in this setting. In our clinical practice we discuss this issue with each patient, making decisions on a case-by-case basis, according to disease history and patient preferences.

Importantly, the practice of using corticosteroids for the treatment of IBD is commonplace and widely accepted. Whereas a placebo-controlled randomized trial showed that corticosteroids may reduce SARS coronavirus clearance,¹¹ other studies have suggested a possible positive influence of these drugs on the SARS outcome because of their potent anti-inflammatory properties.¹² Steroids are currently being used in our country to treat patients with moderate-to-severe CoViD-19, to reduce the signs and symptoms of “super” (severe) inflammation in the later phases of the disease. However, in the early stages (the viral phase of infection) they should be avoided because their use may increase viral burden. The recommendation to reduce as much as possible or discontinue systemic steroids in IBD patients given by the International Organization for the Study of Inflammatory Bowel Disease appears reasonable, but the decision should be made on an individual basis, discussing the benefits and risks with each patient. Of course, steroid tapering (especially if accelerated) should always be conducted under strict medical surveillance, possibly with planned follow-up phone calls and, in any case, ensuring unlimited availability by phone. Again, primary prevention is the most important recommendation we can give to our patients being treated using steroids.

CONDUCTING CLINICAL TRIALS

Another particularly challenging issue we are facing during the CoViD-19 outbreak is conducting clinical trials. Our center normally handles 10-15 ongoing clinical trials, and randomized clinical trials on novel therapeutic compounds are an important resource we use in the management of IBD patients. However, as many of us know, great efforts are commonly required to properly conduct these studies, in compliance with more and more complex protocols. As one may expect, advancing study procedures with a significant reduction of resources has become quite challenging. Still, it is critical for the patients, and for the IBD center, to do whatever is necessary to guarantee continuation of the trial(s) by enrolling patients and avoiding, as much as possible, protocol deviations. Even more so than routine biologic infusions, particular attention should be paid to observing clean pathways and the use of PPE to avoid potential hospital infections. In addition, the reporting

of adverse events should be precise and carefully monitored to separate potential confounding factors because of the current situation. Overall, although we are assuring our patients, particularly those who were already enrolled in clinical trials at the beginning of the coronavirus emergency, that our intent is to continue these studies, at present we are also carefully evaluating any new possible enrollments because of the aforementioned difficulties that may impact our ability to properly conduct these trials.

MANAGEMENT OF IBD RELAPSES

Not only is providing adequate follow-up for chronic diseases such as IBD complicated during the outbreak, but ensuring adequate care of patients with acute conditions is complicated as well. As already mentioned, in many hospitals gastroenterologists have had to be reassigned and are now directly involved in the care of CoViD-19 patients. Even if urgent consults and endoscopic procedures are granted (a 24/7 referral service is maintained for emergent endoscopies), this reorganization adds further difficulties to the management of patients with acute GI diseases who deserve admission. As an example, acute reactivation of IBD has other unique features that may further complicate patient management. First, coronavirus infection may present with GI symptoms, such as diarrhea, weight loss, and abdominal pain, accompanied by mild to moderate fever and no (or mild) respiratory symptoms.¹³ As such, CoViD-19 may mimic IBD relapse symptoms, adding one more diagnostic challenge to this patient population. Moreover, the intense pressure on the emergency system plus patients' fear of being admitted to an “infected” hospital may cause delays in the diagnosis and treatment of acute flares, consequently increasing the risk of medical treatment failure and the need for urgent surgical intervention (eg, in patients with severe ulcerative colitis). In many hospitals, medical and even surgical units have been converted to CoViD-19 units. As such, even if surgeons are still available for urgent cases, another problem to take into account is the availability of ICU beds in hospitals overwhelmed with CoViD-19 patients. In fact, it is very likely that ICUs are completely occupied by critical CoViD-19 patients and that there is no room for “clean” patients.

Considering these difficulties, we preventively assigned a CoViD-19-free hospital with IBD-dedicated gastroenterologists and surgeons, where we can promptly transfer any patients with severe IBD who have a significant risk of needing surgery and who may be admitted to our hospital during the outbreak. We strongly recommend the creation of such networks with surrounding hospitals to select dedicated hubs for the care of specific acute conditions. Cooperation between IBD centers is the key to improving patient outcomes.

CONCLUSIONS

The SARS-CoV-2 pandemic represents one of the most challenging times in the era of modern medicine. As

gastroenterologists, specifically those specializing in IBD, we have to put all our efforts toward protecting our patients during these difficult days. Empowering telemedicine, creating network strategies, and adequately counseling our patients are key measures to overcome this crisis and to create gold-standard strategies for improved care of IBD patients in the future.

REFERENCES

1. Wu F, Zhao S, Yu B, et al. A new coronavirus associated with human respiratory disease in China. *Nature*. 2020;(579):265–269. doi:10.1038/s41586-020-2008-3
2. European Centre for Disease Prevention and Control (ECDC). *Outbreak of novel coronavirus disease 2019 (COVID-19): situation in Italy—23 February 2020*. <https://www.ecdc.europa.eu/en/publications-data/outbreak-novel-coronavirus-disease-2019-covid-19-situation-italy>. Accessed April 10, 2020.
3. Dipartimento della Protezione Civile. *COVID-19 Italia—Monitoraggio della situazione*. <http://opendatadpc.maps.arcgis.com/apps/opsdashboard/index.html#/b0c68bce2cce478eaac82fe38d4138b1>. Accessed April 9, 2020.
4. Mao R, Liang J, Shen J, et al. Implications of COVID-19 for patients with pre-existing digestive diseases [published online ahead of print, 2020]. *Lancet Gastroenterol Hepatol*. 2020;5:426–428. doi:10.1016/S2468-1253(20)30076-5
5. Xiao F, Tang M, Zheng X, et al. Evidence for Gastrointestinal Infection of SARS-CoV-2 [published online ahead of print, 2020 Mar 3]. *Gastroenterology*. 2020;S0016-5085(20)30282-1. doi:10.1053/j.gastro.2020.02.055
6. World Health Organization (WHO). Advice on the use of masks in the community, during home care and in healthcare settings in the context of the novel coronavirus (2019-nCoV) outbreak. WHO. 2020. Retrieved from: [https://www.who.int/publications-detail/advice-on-the-use-of-masks-in-the-community-during-home-care-and-in-healthcare-settings-in-the-context-of-the-novel-coronavirus-\(2019-ncov\)-outbreak](https://www.who.int/publications-detail/advice-on-the-use-of-masks-in-the-community-during-home-care-and-in-healthcare-settings-in-the-context-of-the-novel-coronavirus-(2019-ncov)-outbreak)
7. D'Antiga L. Coronaviruses and immunosuppressed patients. The facts during the third epidemic [published online ahead of print, 2020]. *Liver Transplant*. doi:10.1002/lt.25756
8. Gautret P, Lagier J-C, Parola P, et al. Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. *Int J Antimicrob Agents*. 2020. doi:10.1016/j.ijantimicag.2020.105949
9. Zhang C, Wu Z, Li J-W, et al. The cytokine release syndrome (CRS) of severe COVID-19 and Interleukin-6 receptor (IL-6R) antagonist Tocilizumab may be the key to reduce the mortality. *Int J Antimicrob Agents*. 2020. doi:10.1016/j.ijantimicag.2020.105954
10. Rubin DT, Abreu MT, Rai VSC. Management of patients with Crohn's disease and ulcerative colitis during the COVID-19 pandemic: results of an international meeting. *Gastroenterology*. 2020. doi: 10.1053/j.gastro.2020.04.002.
11. Lee N, Allen Chan KC, Hui DS, et al. Effects of early corticosteroid treatment on plasma SARS-associated Coronavirus RNA concentrations in adult patients. *J Clin Virol*. 2004;31:304–309.
12. Zhao Z, Zhang F, Xu M, et al. Description and clinical treatment of an early outbreak of severe acute respiratory syndrome (SARS) in Guangzhou, PR China. *J Med Microbiol*. 2003;(52(Pt 8)):715–720. doi:10.1099/jmm.0.05320-0
13. Cheung KS, Hung IF, Chan PP, et al. Gastrointestinal manifestations of SARS-CoV-2 infection and virus load in fecal samples from the Hong Kong cohort and systematic review and meta-analysis. *Gastroenterology*. 2020; S0016-5085(20)30448-0. doi:10.1053/j.gastro.2020.03.065