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histological review; therefore, the absence of observed association of CRC in patients with ileocolonic disease location should be interpreted with caution. Patients without defined extent were categorised with patients with L3 (ileoceleal extent), according to the Montreal Classification. Although the Montreal Classification is the standard classification for Crohn's disease distribution in research studies, it does not differentiate the extent of colonic inflammation very well.⁸ Thus, I would not interpret this observation as patients with ileocolonic Crohn's disease not being at risk for CRC. As long as current guideline recommendations have to rely on scant data, I would still include patients with ileocolonic Crohn's disease and involvement of at least a third of the colon in CRC colonoscopy surveillance regimens.

HRs of CRC-associated mortality numerically increased in more recent time periods, between 2003–17. Why was this occurring? It should be noted that the data sources were not consistent during all study periods, with only inpatient data available for earlier time periods (until 2001 in Sweden and 1995 in Denmark), which makes comparisons between time periods difficult. The most recent 2003–17 study period included the early biologic era as well as an early era for colonoscopy surveillance; the absence of reduction in incidence and mortality of Crohn's disease-associated CRC despite improvements in management of Crohn's disease is disappointing. This observation might imply a longer time period of follow-up is needed for improved mucosal inflammation to result in reduction in CRC risk; additional temporal CRC trends in Crohn's disease will need to be studied. Likewise, the effect of colonoscopy surveillance in patients with Crohn's disease, which only occurred towards the end of the study period, will have to be studied further.

This study highlights the subgroup with the highest HR of CRC mortality are patients diagnosed with Crohn's disease before the age of 40 years, compared with

the age-stratified reference population. However, the highest absolute risk of CRC mortality remains among patients over 60 years of age. Despite society guidelines to advocate colonoscopy surveillance in patients with ulcerative colitis and Crohn's disease, rates of colonoscopy surveillance even among high-risk patients with ulcerative colitis and primary sclerosing cholangitis remain abysmal.⁹ Health-care providers need to better communicate risk of CRC to patients with Crohn's disease, and remove barriers to colonoscopy surveillance for patients at risk. Clinical researchers need to further refine their ability to stratify patients most likely to benefit from surveillance resources required for colonoscopy surveillance. To do so, they need more precise means of analysing the extent of Crohn's disease, and they need to identify optimal colonoscopy surveillance intervals, which are currently still undefined.

I declare no competing interests.

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Implications of COVID-19 for patients with pre-existing digestive diseases

The outbreak of coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), first reported in China, in December, 2019, now affects the whole world. As of March 8, 2020, more

than 105 000 laboratory-confirmed cases and more than 3500 deaths in over 100 countries had been reported.

Since SARS-CoV-2 RNA was first detected in a stool specimen of the first reported COVID-19 case in the



Published Online

March 11, 2020

[https://doi.org/10.1016/S2468-1253\(20\)30076-5](https://doi.org/10.1016/S2468-1253(20)30076-5)

For the Chinese translation see

Online for appendix

This online publication has

been corrected. The corrected

version first appeared at

thelancet.com/gastrohep on

May 8, 2020

USA,¹ much attention has been paid to the study and reporting of gastrointestinal tract infection of SARS-CoV-2. According to a study² including 1099 patients with laboratory-confirmed COVID-19 from 552 hospitals in China as of Jan 29, 2020, nausea or vomiting, or both, and diarrhoea were reported in 55 (5.6%) and 42 (3.8%) patients. Autopsy studies are crucial to help understand the involvement of COVID-19 in the digestive system; however, to date, there has been only one autopsy report³ for a man aged 85 years with COVID-19, which showed segmental dilatation and stenosis in the small intestine. Whether this finding is

secondary to COVID-19 or a pre-existing gastrointestinal comorbidity is unknown.

COVID-19 has implications for the management of patients with pre-existing digestive diseases. Indeed, the presence and number of comorbidities is associated with poorer clinical outcome in patients with COVID-19. In the study² of 1099 patients with laboratory-confirmed COVID-19, 261 (23.7%) patients with COVID-19 reported having at least one comorbidity, with hypertension, diabetes, and coronary heart disease being the most common. In this study,² 23 (2.1%) patients had hepatitis B infection; chronic hepatitis B infection did not seem to be associated with a severe course of COVID-19.² Abnormal liver function tests, including elevated aspartate aminotransferase, alanine aminotransferase, and total bilirubin were noted.² Liver abnormalities in patients with COVID-19 might be due to viral infection in liver cells but could also be due to other causes such as drug toxicity and systemic inflammation.⁴ Data suggest that liver injury is more prevalent in severe cases than in mild cases of COVID-19.⁴ However, data about other underlying chronic liver conditions such as non-alcoholic fatty liver disease, alcohol-related liver disease, and autoimmune hepatitis, and their effect on prognosis of COVID-19 needs to be further evaluated.

Liver transplantation might involve a risk of transmission of viral infection from donor to recipient, as shown in the previous SARS outbreak, and therefore donor screening and testing is crucial.⁵ Although many patients had comorbidities in the reported series,² none had been a transplant recipient. Transplant clinicians are encouraged to follow guidance issued by The Transplantation Society,⁶ as well as local health department guidelines for isolating, quarantining, testing, and monitoring returned travellers from endemic areas.

Patients with cancer in general are more susceptible to infection due to their immunocompromised status caused by the malignancy and anticancer treatments. However, whether patients with gastrointestinal cancers are more likely to be infected with SARS-CoV-2 than healthy individuals remains unknown. In a recent nationwide analysis from China,⁷ 18 (1%) of 1590 COVID-19 cases had a history of cancer. Among these 18 cases, three had a history of colorectal cancer (one colonic tubular adenocarcinoma, one rectal

Panel: Key recommendations for managing patients with IBD during the COVID-19 epidemic

Potential risk factors for SARS-CoV-2 infection

- Patients with inflammatory bowel disease (IBD) on immunosuppressive agents
- Patients with active-stage IBD with malnutrition
- Elderly patients with IBD
- Patients with IBD frequently visiting medical clinic
- Patients with IBD with underlying health conditions, such as hypertension and diabetes
- Patients with IBD who are pregnant

Medication for patients with IBD

- Continue current treatment if disease is stable, and contact your doctor for suitable medicine if disease has flared
- Use of mesalamine should be continued and should not increase the risk of infection
- Corticosteroid use can be continued, but be cautious of possible side-effects
- A new prescription of immunosuppressant or increase in dose of an ongoing immunosuppressant is not recommended in epidemic areas.
- Use of biologics such as the anti-TNFs infliximab or adalimumab should be continued
- If infliximab infusion is not accessible, switching to adalimumab injection at home is encouraged
- Vedolizumab use can be continued due to the specificity of the drug for the intestine
- Ustekinumab use can be continued, but starting ustekinumab requires infusion centre visits and therefore is not encouraged
- Enteral nutrition might be used if biologics are not accessible
- Tofacitinib should not be newly prescribed in epidemic areas unless there are no other alternatives

Surgery and endoscopy

- Postpone elective surgery and endoscopy
- Screening for COVID-19 (complete blood count, IgM or IgG, nucleic acid detection, and chest CT) before emergency surgery

Patients with IBD and fever*

- Contact your IBD doctor about potential option to visit fever outpatient clinic with personal protection provisions if temperature continues over 38°C
- Suspend the use of immunosuppressant and biological agents after consultation with your IBD doctor, and follow appropriate local guidance for suspected COVID-19 if COVID-19 cannot be ruled out

COVID-19=coronavirus disease 2019. SARS-CoV-2=severe acute respiratory syndrome coronavirus 2. *Fever is the most common reported symptom in COVID-19.

carcinoma, and one colorectal carcinoma).⁷ Patients with COVID-19 and cancer were observed to have a higher risk of severe events; several strategies have been proposed, such as intentional postponing of adjuvant chemotherapy or elective surgery on a patient-by-patient basis, stronger personal protection provisions, and more intensive surveillance or treatment.⁷

Given the use of biologics and immunosuppressive agents, whether patients with inflammatory bowel disease (IBD) are more susceptible to SARS-CoV-2 infection has raised great concern. Currently no patients with IBD have been reported to be infected with SARS-CoV-2 in the IBD Elite Union, which incorporates the seven largest IBD referral centres in China with more than 20 000 patients with IBD.⁸ Furthermore, no patients with IBD with SARS-CoV-2 infection have been reported from the three largest tertiary IBD centres in Wuhan (Tongji Hospital, Union Hospital, and Zhongnan Hospital) at the time that this manuscript was prepared (March 8, 2020).

Several strategies have been implemented in China to minimise the potential risk of SARS-CoV-2 infection in patients with IBD since the outbreak of COVID-19. First, the Chinese IBD Society issued official guidelines for managing patients with IBD in early February 2020.⁹ The guidelines include practical recommendations on the use of immunosuppressive agents and biologics, diet, and intentional postponement of elective surgery and endoscopy, as well as personal protection provisions; these are outlined in the panel. Second, the China Crohn's & Colitis Foundation has organised a group of volunteer gastroenterologists that specialise in IBD to offer online consultancy to patients with IBD since Jan 29, 2020. Third, an online virtual IBD visit programme has been initiated in some IBD centres, which provides convenient and cost-effective care, and could potentially reduce the risk of SARS-CoV-2 infection by avoiding close contact with infected patients in public areas. With the increasing concern from patients with IBD globally, helpful online resources about COVID-19 have been provided by international non-profit organisations such as Crohn's Colitis of Foundation America and Crohn's & Colitis UK.^{10,11} Such guidance and advice should be delivered urgently to health-care workers as well as patients with IBD.

The comorbidity spectrum of digestive conditions and its impact on treatment and outcome of COVID-19

remains largely unknown. Further data need to be analysed from the COVID-19 cohort established by the National Health Commission of the People's Republic of China, which would help to more precisely ascertain the risk of SARS-CoV-2 infection in patients with digestive comorbidities such as IBD. These data and experience with guidance on how to manage patients with underlying comorbidities in China could facilitate integrated care for patients globally.

We declare no competing interests. We thank the members of Chinese IBD Elite Union, Chinese Society of IBD and Chinese IBD Quality Care Evaluation Center Committee (IBDQCC) for their collaboration. RM and JL contributed equally.

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