Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

expectation of 50% improvement at 12 weeks might not have been reasonable to assess the additional benefit of palliative radiotherapy. This limitation suggests that perhaps the initially planned endpoint was better suited to answer the study question, although it was unachievable because of difficulties with recruitment and patient deterioration.

The ROCS trial provides valuable data and alerts us that routine use of SEMS plus palliative radiotherapy is not indicated for patients with advanced oesophageal cancer, except for patients with high upper gastrointestinal bleeding risk. It also underscores the importance of patient selection in determining both which and how many modalities are offered to manage dysphagia associated with advanced oesophageal cancer.

We declare no competing interests.

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

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The risk of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and development of severe COVID-19 in patients with pre-existing digestive diseases has raised great concern since infection of the gastrointestinal tract was first reported in March, 2020.[1] In addition, patients with pre-existing digestive diseases are thought to be at increased risk of infection due to immune dysfunction.[2] In response, we published a Comment in *The Lancet Gastroenterology & Hepatology* on the implications of COVID-19 for such patients during the early stages of the pandemic.[3] Our knowledge about COVID-19 has continued to expand, and we provide an updated overview of the implications of COVID-19 for patients with pre-existing digestive diseases.

Few studies assessing the risk of SARS-CoV-2 infection in patients with pre-existing digestive disease have included suitable control groups. A study using national data from the US Department of Veterans Affairs health-care system included 88 747 veterans tested for SARS-CoV-2 before May 15, 2020, and suggested that there was no difference in likelihood of testing positive for SARS-CoV-2 between those with and without a diagnosis of cirrhosis after adjustment for sociodemographic characteristics, comorbidities, and presenting symptoms.[4] Two international registries—COVID-Hep and SECURE-Cirrhosis—were created to collate data from COVID-19 cases in patients with chronic liver diseases and liver transplant recipients. An analysis of 745 patients with chronic liver diseases with SARS-CoV-2 infection showed that baseline liver disease stage and alcohol-related liver disease were independent risk factors for death from COVID-19.[5]

There is no definitive evidence regarding infection risk in solid organ transplant recipients compared with patients without a transplant. A nationwide population

study in Italy found that the cumulative incidence of SARS-CoV-2 infection was higher in transplant recipients than in patients who had not had a transplant.[6] When stratified by type of organ transplant, the cumulative incidence was higher for heart transplants and lower for liver transplants versus kidney transplants.[6] However, more organ transplant recipients had two or three comorbidities than did the control population.[6] An analysis of 151 liver transplant recipients with SARS-CoV-2 infection in the COVID-Hep and SECURE-Cirrhosis registries showed that liver transplantation was not independently associated with death, whereas known risk factors, such as increased age and presence of comorbidities were.[7] For liver transplant recipients, most societies, such as the American Association for the Study of Liver Diseases and European Association for the Study of the Liver, advise against reducing immunosuppressive therapy to prevent SARS-CoV-2 infection. Reduction should only be considered under special circumstances (eg, medication-induced lymphopenia, or bacterial or fungal superinfection in case of severe COVID-19) after consultation with specialists.[8,9]

Data linking pre-existing non-alcoholic fatty liver disease (NAFLD) with SARS-CoV-2 infection are scarce. A retrospective analysis of a large electronic health record database including 61·4 million adults showed that the cumulative incidence of COVID-19 was higher in patients with a primary diagnosis of metabolic syndrome (0·10% *vs* 0·01%, odds ratio [OR] 7·00 [95% CI 6·11–8·01]) than in patients without metabolic syndrome. The adjusted OR (aOR) of having COVID-19 was higher in patients if they were diagnosed with non-alcoholic steatohepatitis (aOR 4·93 [95% CI 4·06–6·00]) than if they were not.[10] Moreover, NAFLD was independently associated with COVID-19 progression.[11]

Whether patients with inflammatory bowel disease (IBD) are more susceptible to SARS-CoV-2 infection was a crucial question at the beginning of the pandemic. Several large cohort studies have provided epidemiological evidence that patients with IBD, including those receiving biologics or immunosuppressive medications, do not seem to have an increased risk of SARS-CoV-2 infection compared with the general population. For instance, a population-based cohort in the Netherlands showed that the incidence of COVID-19 in patients with IBD was similar to that of the general population.[12]

An early report from the SECURE-IBD registry showed that corticosteroids and aminosalicylates were associated with an increased risk of severe COVID-19, whereas TNF antagonists were not.[13] An update in June, 2020, showed that combination therapy and thiopurines might be associated with an increased risk of severe COVID-19 compared with TNF antagonists.[14] Similarly, even when corrected for age, patients who used aminosalicylates had an increased risk of severe COVID-19 compared with patients who did not use aminosalicylates (many of whom used TNF antagonists). Thus, it is still unclear whether immunomodulator or aminosalicylates use truly confers increased risk of severe COVID-19, or whether TNF antagonists reduce the risk of severe COVID-19. Notably, no significant differences were observed when comparing classes of biologics.[14] Overall, the implications of these findings are still debated, due to study design and selection bias in such observational registries.

Given the potential risk of discontinuing IBD medications, such as disease flare and other complications, expert gastroenterology societies recommend continuation of medications except corticosteroids. Patients receiving a combination of two immunosuppressive drugs, such as thiopurine and a TNF antagonist, should discuss with their doctor if the combination therapy could be de-escalated.

Due to an unprecedented international effort, safe and effective vaccines against SARS-CoV-2 are being administered worldwide. Although the mRNA vaccines have not been tested in immunosuppressed populations such as those with IBD or chronic liver diseases, they do not contain live or live-attenuated viruses and are therefore not considered to pose infective risk. Most experts currently advocate vaccinating immunocompromised populations with the mRNA vaccines, including patients with IBD receiving biologics and immunosuppressive agents, because the vaccines have been shown to be efficacious and safe in the general population and the risk of COVID-19 complications in immunocompromised populations exceeds the uncertainty on vaccine safety in these groups. Similarly, other SARS-CoV-2 vaccines—eg, replication-incompetent vector vaccines, inactivated vaccines, and recombinant vaccines—are also considered to be safe to administer to patients with IBD. Vaccine efficacy might be decreased in patients with

chronic liver disease, IBD, or after liver transplantation, but most vaccines are generally recommended for these patients. Physicians should counsel patients that there is a possibility of reduced vaccine efficacy when receiving systemic corticosteroids. Further studies are necessary to document the immunogenicity to mRNA vaccines in immunosuppressed populations.

Outstanding questions pertinent to patients with pre-existing digestive condition include the long-term effect of COVID-19 on the natural history of digestive diseases, degree of immunity and risk of SARS-CoV-2 reinfection, the safety of emerging vaccines, whether biologics and immunosuppressive drugs influence the effectiveness of the SARS-CoV-2 vaccine, and the duration of vaccine-induced immunity. These points will need to be addressed by the medical community in the near future.

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Relevance of reproductive health to comprehensive hepatology care

In the USA, chronic liver disease is the sixth most common cause of mortality in young women aged 20–44 years.[1] Moreover, non-alcoholic fatty liver disease, which is now the leading cause of chronic liver disease in the USA, has seen the most marked rise in incidence in young adults compared with other age groups.[2] These epidemiological trends are consistent with pregnancy data showing a near tripling of the prevalence of non-alcoholic fatty liver disease in pregnancy over the past decade, and an increase in alcohol-related liver disease in women of reproductive age.[3,4] In light of this growing population, hepatology providers must now address