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pancreatitis was also found in 2 family clusters with SARS-CoV-2 infection.⁵ Furthermore, SARS-CoV-2 RNA was detected in the pancreatic pseudocysts of a patients with COVID-19.⁶ In the Giuseppe et al⁷ study of 70 COVID-19 cases, 6 (8.5%) demonstrated pancreatic abnormalities with significant evaluations of serum PE activity. Mechanistically, it had been found that angiotensin-converting enzyme 2 (ACE2), receptor of SARS-CoV-2, was more highly expressed in the pancreas than the lungs.⁸ Studies further demonstrated that ACE2 and transmembrane serine protease 2 were prominently expressed in pancreatic ductal epithelium and microvasculature.^{9,10} Moreover, the autopsies of 3 COVID-19 cases showed degeneration of islet cells.¹¹ In addition, ACE2 and transmembrane serine protease 2 were found to be highly expressed in gastrointestinal epithelial cells, and the virus could be detected in stools. Thus, SARS-CoV-2 might infect the pancreas by spreading from duodenal epithelium to pancreatic ductal epithelium. Most importantly, during the outbreak of another coronavirus (SARS-CoV) in 2003, its antigen and RNA were detected in pancreatic cells.¹² Collectively, these results indicated the pancreas as a potential target of SARS-CoV-2.

In addition, viral sepsis was hypothesized in the COVID-19 progression.¹³ Severe SARS-CoV-2 infection could cause alveolar macrophages or epithelial cells to produce various proinflammatory cytokines and chemokines and led to uncontrolled inflammation cascade and cytokine storm. Meanwhile, severe endotheliitis directly induced by SARS-CoV-2 could further cause diffuse microischemic disease in the pancreas.¹⁴ Thus, the disseminated SARS-CoV-2 could also directly attack multiple other organs, including the pancreas. Eventually, viral sepsis, ischemic damage, and multiple organ failure occurred. Furthermore, up to 16% of patients with severe COVID-19 had elevated PE levels and 7% showed significant changes in the pancreas on computed tomography, but fewer than 2% in patients with non-severe COVID-19.⁸ Taken together, we must pay attention to potential pancreatic injuries during the management of COVID-19.

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Conflicts of interest

The authors disclose no conflicts.

Most current article

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The Courage to Return to Everyday Life at the Time of COVID-19: The Point of View of Inflammatory Bowel Disease Patients Needing Endoscopy



Dear Editors:

We read with interest the paper by Rex et al¹ on the willingness of patients to undergo elective endoscopic procedures after lockdown due to the Coronavirus Disease 2019 (COVID-19) pandemic. The authors reported that only 4.3% of surveyed patients were unwilling to undergo elective endoscopy in May 2020. Due to the COVID-19 pandemic, there was a huge increase in the number of hospitalized patients, which overloaded health systems and caused the dramatic shortage of health resources² and the consequent scarcity of medical assistance among acute and chronic diseases. This led to a forced stop or a significant limit on health system offer, including elective outpatient endoscopic procedures also in patients with inflammatory bowel diseases (IBD).³ Alternative methods of disease assessment, including biomarkers or telephone/email helpline to support patients with disease flares, were suggested.³ These restrictive measures help to keep patients at home but may lead to an excessive use of corticosteroids, which could worsen the course of any eventual COVID-19 infection,⁴ or they could delay the start of biological therapies with related consequences.⁵ As it is uncertain how long the COVID-19 pandemic will last, we do not know if a prolonged period without endoscopy may result in long-term implications for patients with IBD who need to monitor efficacy of treatments or be screened for dysplasia and colorectal cancer.⁶ Therefore, a gradual return to routine

endoscopic activity is desirable because direct examination of the mucosal surface and tissue acquisition are fundamental both for the diagnosis^{6,7} and management of IBD.³

The point of view of patients undergoing endoscopic procedures during the COVID-19 pandemic and post-pandemic period should be evaluated. Considering this issue, we conducted a survey on patients whose scheduled elective colonoscopies were cancelled during lockdown, between March 8 and May 25, 2020. The survey was carried out by contacting 118 patients by phone: 2 patients (1.7%) refused to participate, so we continued with 116 (98.3%) who completed the interview. Among these, 60 were men (51.7%) and 56 (48.3%) women, with an overall mean age of 45.6±15.3 years. Sixty (51.7%) of 116 patients had Crohn's disease, and 56 (48.3%) had ulcerative colitis. Twenty-two patients (19.0%) reported a disease flare at the time of the interview, and 94 (81.0%) were in clinical remission. None of the surveyed patients (or their family members) reported a COVID-19 infection. When asked if they feared COVID-19 contagion, 108 (93.1%) of 116 patients said "Yes" and the remaining 8 patients (6.9%) said they were not afraid. Interestingly, patients with a lower educational level as well as those treated with immunosuppressants or biologics were more frightened ($P = .042$ and $P = .008$, respectively). When asked if they were willing to undergo endoscopic procedures the following month, 106 patients (91.4%) agreed and 10 (8.6%) refused. Among those who agreed to undergo colonoscopy, 102 (96.2%) of 106 patients wished to perform the procedure after discussion with their gastroenterologist and in a referral center equipped to prevent COVID-19 infection. Patients with a symptomatic disease flare at the time of the interview were more emphatic about prevention measures ($P = .001$). Age, gender, marital status, and having children at home did not influence their concern about COVID-19 infection or their unwillingness to undergo the endoscopic procedure.

In conclusion, results show that most of the patients with IBD are willing to undergo endoscopy provided the indication for the examination is discussed beforehand with the gastroenterologist and the procedure is carried out in a referral center. A lower level of education and immunosuppressants or biological treatment can affect patients' feelings about the risk of COVID-19 contagion. Among patients who accepted endoscopy, their symptomatic disease flare was related to their request for a center equipped to prevent COVID-19 infection. Certainly, detailed plans and suggestions on how to deal with the long waiting lists resulting from the lockdown are necessary.⁷ As the number of endoscopic procedures to be scheduled is excessive, it will take time to return to pre-pandemic levels, so patients should be carefully selected and stratified according to their symptoms, over the next few months. It is crucial that, even reaching an adequate number of procedures, all endoscopies are performed following the current recommendations for endoscopic procedures during COVID-19, including personal protective equipment.⁸

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The Pi**MZ* Allele in Alpha-1 Antitrypsin Increases Liver-Related Outcomes in a Population-Based Study



Dear Editors:

We read with great interest the article by Schneider et al¹ on the effect of the Pi**Z* allele in alpha-1 antitrypsin peptide (*AAT*) on liver phenotypes that, contrary to current dogma, demonstrated that heterozygous Pi**Z* allele carriers are also at risk for liver disease. However, limitations raised by the authors themselves include the cross-sectional study design, with inability to prove cause-and-effect relationships, and potential selection bias. The authors call for large longitudinal population-based studies with clinical liver-related outcomes to overcome these limitations and validate their findings.

Here, we studied the association of the Pi**Z* variant with clinical liver-related outcomes and non-liver-related death in large and representative Finnish general population cohorts (FINRISK 1992-2012 and Health 2000)^{2,3} with long-term linkage to national registers until 2015 for hospital admissions, cancer, and death as previously described.⁴ After excluding 8 homozygous Pi**Z* allele carriers, our