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.

retrospective design of our study, monitoring strategies for these patients were at the discretion of the physician. Results of gastroscopy were not taken into account at study inclusion or during follow-up evaluation.

In the CREOLEstudy, to our knowledge, no data on mucosal healing was available during follow-up evaluation. Endoscopic stricture, as defined by the CDEIS score, could persist in the group with clinical success. In our study, few patients had structuring disease, respectively, 1 (1.8%) patient in the CDEIS = 0 group compared with 4 (14.8%) patients in the CDEIS >0 to <4 group. In univariate analysis, both stricturing phenotype (hazard ratio [HR], 4.26; 95% CI, 1.33–13.69; $P = .0149$) and CDEIS >0 and <4 vs CDEIS = 0 (HR, 2.17; 95% CI, 1.01–4.65; $P = .047$) were associated with treatment failure. However, in multivariate analysis, only CDEIS >0 and <4 vs CDEIS = 0 was associated independently with treatment failure (HR, 2.17; 95% CI, 1.01–4.65; $P = .0204$).

Last, results of therapeutic drug monitoring and calprotectin were not available. This study was retrospective and included patients between 2008 and 2015, mainly before the diffusion of these new monitoring tools in clinical practice.

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Conflicts of interest
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Most current article

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SARS-CoV-2-Induced Pancreatitis is a Rare but Real Entity

Dear Editor:

We read with great interest the letter by Ramsey et al[1] in which they present original data on hyperlipasemia in 1992 patients with coronavirus disease 2019 (COVID-19) from 36 medical centers. Of 400 patients with hyperlipasemia, they found only 2 patients who presented with pancreatitis of which both had a biliary etiology. They found an additional 6 that were diagnosed with pancreatitis during the hospital stay and were attributed to COVID-19. They conclude that most COVID-19 patients with hyperlipasemia are likely from critical illness and not pancreatitis; and that the cause of pancreatitis needs investigation when present.

Although the results of the study are interesting, we find 2 methodologic flaws that make this report hard to draw conclusions from. First, when studying the prevalence of a disease (pancreatitis) that we know is infrequent, it would be ideal to report on 1 large population. In this study, several small populations are combined to form the dataset (around 55 patients a center). Statistically this is not ideal to evaluate the prevalence of an uncommon disease. Second, a study evaluating the causative role of pancreatitis in COVID-19 should have a control group with patients without COVID-19.

Two recent studies report on this topic. A large single health system retrospective study examined 48,012 hospitalized patients in New York, of which 11,883 were COVID positive.[2] Of the total population, 189 met criteria for pancreatitis (a strict criteria of 3/3 Atlanta classification was required) on admission of which 32 were COVID-19 positive. Among patients with COVID-19, the most common etiology was idiopathic at 69%, compared with 21% in patients who were COVID-19 negative ($P <$ .0001). These data implicate SARS-CoV-2 in a possible causative role and shows COVID-19 can present as pancreatitis. Another study from 1 large health system in Minnesota found similar results when comparing patients with pancreatitis with and without COVID-19. Patients with COVID-19 and pancreatitis had an idiopathic etiology in 57% of cases compared with 2% on patients without COVID-19.[3]

We do agree with Ramsey et al[1] in that patients with a serum lipase less than 3 times the upper limit of normal and who do not meet Atlanta criteria have lipase elevations likely from critical illness. We examined this cohort in our large health system and also found this association.[4] Not surprisingly, patients with pancreatitis had better outcomes than those with critical illness.

We believe there are 3 groups of patients with COVID-19 who could have elevated lipase: (1) critically ill patients in whom lipase is <3 upper limit of normal; (2) critically ill patients in whom lipase is >3 upper limit of normal, but do not meet criteria for pancreatitis (as per Atlanta criteria); and (3) patients with pancreatitis who meet Atlanta criteria (with known etiology of pancreatitis and also idiopathic pancreatitis that might be caused by COVID-19 infection).

In conclusion, pancreatitis caused by SARS-CoV-2 is a real but rare entity; in fact COVID-19 can present as pancreatitis. Sufficient evidence exists to implicate SARS-CoV-2 in a causative role. Patients should meet the Atlanta classification for pancreatitis. Hyperlipasemia in

COVID-19 not meeting the definition of pancreatitis is likely from critical illness.

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Conflicts of interest
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Most current article

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Lessons Learned From Two Prematurely Terminated, Randomized Trials on Biliary Drainage in Perihilar Cholangiocarcinoma

Dear Editor:

The recently published INTERCPT-study was after the DRAINAGE-study, the second randomized controlled trial that compared endoscopic biliary drainage versus percutaneous biliary drainage in patients with perihilar cholangiocarcinoma (PHC).[1,2] Unfortunately, both studies have been prematurely stopped, raising several concerns.

The INTERCPT-study was started in October 2017 and stopped in March 2019 by the Data Safety Monitoring Board because of slow accrual. In 18 months, only 13 patients were included out of 51 screened individuals among 16 centers in the United States, while the calculated sample size was 184. The authors described several factors that may have caused slow enrollment; many patients had been referred after initial drainage had already been undertaken, precluding enrollment in the trial. This was also encountered in the Dutch multicenter DRAINAGE-trial, which also randomized patients with PHC to endoscopic biliary drainage or percutaneous biliary drainage.[2] This trial was stopped because of higher overall mortality in the percutaneous biliary drainage group. Within a 2.5-year period, 54 out of 261 screened patients could be included. A national, multidisciplinary clinical pathway, succeeded in more patients being referred to our center without previous biliary drainage. We believe that awareness among gastroenterologists and surgeons in referring centers of assessment of imaging before inserting biliary drains, is key to staging and to devising a treatment strategy.

Although both randomized trials had the same objective (ie, to identify the optimal, initial biliary drainage technique in PHC), primary endpoints differed. In the INTERCPT-study, the primary endpoint was successful biliary drainage, defined as 50% reduction in bilirubin level within 3 weeks without additional drainage procedures. In the DRAINAGE-trial, the primary outcome was the number of severe complications of biliary drainage occurring between randomization and surgery. Therapeutic success was a secondary endpoint and was defined as normal-caliber bile ducts on ultrasound and a 20% decrease in bilirubin level within 1 week. Although difficult to compare because of different definitions, therapeutic success of biliary drainage was achieved in 6 out of 13 patients (46%) in the INTERCPT-study versus 38 out of 54 patients (70%) in the DRAINAGE-trial.

Remarkably, the high mortality rate in the DRAINAGE-trial led to early study termination, whereas high mortality and complication rates were also observed in the INTERCPT-study: 10 of 13 patients (77%) experienced adverse events requiring hospital admission (vs 65% in the DRAINAGE-trial) and 8 of 13 patients (62%) died within 3 months follow-up (vs 26% in the DRAINAGE-trial). The unexpectedly high mortality rates in both trials require special attention. In the DRAINAGE-trial, with an all-cause mortality design, mortality seemed unrelated to drainage in 5 of 14 patients (2 myocardial infarction and 3 disease progression). Six patients died because of postoperative complications. The causes of death in the INTERCPT-trial have not been specified.

An important difference between both trials was that the DRAINAGE-trial included patients with tumors deemed resectable, whereas the INTERCPT-study also included patients requiring biliary drainage in the palliative setting. This may have resulted in an even more heterogenous and complex trial population, hampering conduct and progress of this study. The authors of the INTERCPT-study encountered logistic issues in enrolling patients on-site and that institutional/clinician bias in favor of 1 of the 2 drainage techniques prevailed. The DRAINAGE-trial was conducted in 4 Dutch tertiary centers, whereas the INTERCPT-trial included 16 centers scattered among the United States. Effective collaboration among surgery, gastroenterology, and interventional radiology departments is more likely in a limited number of dedicated, participating centers.

Remarkably, 2 randomized studies including patients with PHC both showed outcomes that contradict only retrospective data available in literature. Especially in