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Low Incidence of Severe Gastrointestinal Complications in COVID-19 Patients Admitted to the Intensive Care Unit: A Large, Multicenter Study



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Patients hospitalized with Coronavirus Disease 2019 (COVID-19) often have gastrointestinal symptoms, including diarrhea, nausea, vomiting, and abdominal pain.¹ However, the rate of gastrointestinal complications in patients with COVID-19 is less well described. Recent reports from a single center have suggested an alarmingly high rate of serious gastrointestinal complications in critically ill patients with COVID-19.^{2,3} In a retrospective review of 92 patients with severe COVID-19 admitted to the intensive care unit (ICU), 44 patients (48%) had ileus, 4 (4%) had intestinal ischemia, and 2 (2%) had Ogilvie syndrome.² Several other case reports have described intestinal ischemia in the setting of COVID-19.⁴ However, reports from single centers should be interpreted with caution because of small sample sizes and limited generalizability to patients from wider geographic distributions. The aim of this study was to assess the rate of serious gastrointestinal complications in patients with COVID-19 admitted to the ICU in a large, geographically diverse sample.

Methods

Study Design

This study analyzed data from a cohort of patients with COVID-19 who were hospitalized at 36 medical centers in the United States and Canada. The institutional review board at each participating center approved the study.

Study Patients

The first 50 to 100 consecutive adult (age ≥ 18 years) patients with a confirmed diagnosis of COVID-19 were enrolled from each center. For each patient, all available relevant clinical data (symptoms, laboratory and imaging results, clinical notes, and endoscopic findings) were collected by review of electronic health records. Demographic and hospitalization characteristics, including length of hospital stay, ICU stay, and discharge disposition also were recorded. Data were collected between April 15 and June 5, 2020, and entered into a secure electronic database.

Outcomes

The primary outcome of this study was the rate of any severe gastrointestinal complication. The hepatic complication of interest was severe liver enzyme elevation (alanine aminotransferase elevation >1000 unit/L). Gastrointestinal complications included any significant luminal and pancreaticobiliary medical or surgical disorder such as acute pancreatitis, acute cholecystitis, acute mesenteric ischemia, intestinal obstruction, gastrointestinal infections (eg, *Clostridioides difficile*), and gastrointestinal bleeding requiring endoscopic evaluation or intervention.

Statistical Analysis

Data were analyzed using descriptive statistics, with categorical variables summarized using proportions and continuous variables summarized using means with standard deviation or medians with interquartile range. All data analyses were conducted using SAS 9.4 (SAS Institute, Inc., Cary, NC).

Results

Data were collected for 1992 patients who were hospitalized with COVID-19. Of these, 878 patients were admitted to the ICU. Demographics, clinical characteristics, and outcomes of the study cohort are described in Table 1. The mean age of patients was 61.9 years (standard deviation 15.1) and 61.8% were men. The most common comorbidities were hypertension (67.7%), diabetes mellitus (40.8%), pulmonary disease (31%), and cardiac disease (25.2%). Eighty patients (9.1%) had prior gastrointestinal or liver disease. Overall, 634 patients (72.2%) required mechanical ventilation, and 534 (60.8%) required vasopressor support, and 299 patients (34.1%) died during their hospitalization.

Severe gastrointestinal complications occurred in 45 patients (5.1%), most of which were elevated alanine aminotransferase >1000 U/L in 22 (2.5%) patients. Ten patients (1.1%) developed gastrointestinal bleeding requiring endoscopic evaluation. There were 6 cases of C

Abbreviations used in this paper: COVID-19, Coronavirus Disease 2019; ICU, intensive care unit.

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Table 1. Characteristics and Gastrointestinal Complications in Patients With COVID-19 Admitted to the Intensive Care Unit (n=878)

Patient characteristics	
Age, ^a mean (SD)	61.9 (15.1)
Sex	
Male	543 (61.8)
Female	335 (38.2)
Cigarette smoking	
Current smoker	50 (5.7)
Ex-smoker	281 (32)
Nonsmoker	482 (54.9)
Unknown	65 (7.4)
Alcoholism	
Current	73 (8.3)
Prior	41 (4.7)
None	644 (73.4)
Unknown	120 (13.7)
Obesity	463 (52.7)
Body mass index, ^b mean (SD)	32.2 (9.1)
Hypertension	594 (67.7)
Diabetes	358 (40.8)
Pulmonary disease	272 (31)
Cardiac disease	221 (25.2)
Prior or current cerebrovascular accident	84 (9.6)
Peripheral vascular disease	44 (5)
Active/current malignancy, excluding nonmelanoma skin cancer	59 (6.7)
Prior gastrointestinal disease	80 (9.1)
Luminal gastrointestinal disease (nonmalignant)	28 (3.2)
Pancreaticobiliary disease	28(3.2)
Chronic liver disease	28(3.2)
Outcomes	
Hospital length of stay, days, median (IQR)	16 (9–26)
Intensive care unit length of stay, d, median (IQR)	9 (5–17)
Mechanical ventilation	634 (72.2)
Vasopressor support	534 (60.8)
Death	299 (34.1)
Severe gastrointestinal complications ^c	45 (5.1)
Luminal and pancreaticobiliary	24 (2.7)
Severe gastrointestinal bleeding	10 (1.1)
Acute pancreatitis	1 (0.1)
Acute cholecystitis	2 (0.2)
Small bowel obstruction	1 (0.1)
Ogilvie syndrome	2 (0.2)
Mesenteric ischemia	2 (0.2)
<i>Clostridioides difficile</i> infection	6 (0.7)
Hepatic	
Elevated ALT >1000 U/L	22 (2.5)

NOTE. Values are n (%) unless otherwise noted. ALT, alanine aminotransferase; IQR, interquartile range; SD, standard deviation.

^aAge was not collected for patients >89 years old.

^b52 missing.

^cOne patient had gastrointestinal bleeding and ALT >1000 IU/L.

difficile infection, 2 cases of acute mesenteric ischemia, 2 cases of acute colonic pseudoobstruction (Ogilvie syndrome), and 2 cases of acute cholecystitis. One patient had acute pancreatitis and 1 patient developed small bowel obstruction due to incarcerated inguinal hernia. Of the 2 cases with mesenteric ischemia, 1 patient developed severe diffuse colonic ischemia requiring a colectomy and was discharged alive, and the other patient developed small and large bowel ischemia and pneumatosis and died during the hospitalization. Of those with severe gastrointestinal complications, 25 (55.6%) died during the hospitalization.

Discussion

In this study, we found an overall low rate (5.1%) of severe gastrointestinal complications in patients with COVID-19 admitted to the ICU. Most of these complications were related to severe liver enzyme elevation (48.9%, or 2.5% of overall population), followed by gastrointestinal bleeding (22.2%, or 1.1% of all patients) and *C difficile* infection (13.3%, or 0.7% of all patients). The rate of other luminal and pancreaticobiliary complications was very low.

In particular, the rate of intestinal ischemia, previously reported to be in excess of 4%,² was only 0.2% in this cohort. It is increasingly apparent that COVID-19 represents a hypercoagulable disorder that is associated with a higher incidence of venous thromboembolism. In addition, severe acute respiratory syndrome coronavirus 2 has been found to infect the endothelial cells of different vascular beds in the heart, small bowel, and lungs.⁵ Therefore, it is postulated that endotheliitis caused by COVID-19 leads to microthrombus formation and organ ischemia. However, consistent with our findings, a recent study of 3089 patients with COVID-19 infection at 2 hospitals in Spain found that only 12 patients (0.4%) required surgical consultation, of whom 4 patients (0.13%) developed bowel ischemia and perforation.⁶ Similarly, a multicenter prospective cohort study from France that evaluated the rate of thrombotic complications in 150 patients with COVID-19 admitted to the ICU found that although 64 patients (42.7%) developed clinically relevant thrombotic complications, only 1 (0.7%) developed mesenteric ischemia.⁷

In conclusion, in this multicenter study involving a large number of ICU patients with COVID-19 across North America, we found a low incidence of severe gastrointestinal complications, consistent with rates reported in critically ill patients in general.⁸ Despite recent reports of increased risk of intestinal ischemia in patients with COVID-19, our study found a low rate of this complication and therefore provides reassurance that this phenomenon may not be as problematic as initially believed.

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Conflict of interest

The authors disclose no conflicts.

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