

## **Gastrointestinal Complications in Critically III Patients with COVID-19**

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#### **TEXT**

Extra-pulmonary disease has been observed in patients with Coronavirus Disease 2019 (COVID-19) (1-3). We describe here the gastrointestinal (GI) complications of patients with severe COVID-19 admitted to the intensive care unit (ICU) at the Massachusetts General Hospital between March 13<sup>th</sup> and April 12<sup>th</sup>, 2020.

During this time period, 141 patients were admitted to the ICU with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection confirmed by reverse-transcriptase—polymerase-chain-reaction (RT-PCR) testing. The median (interquartile range [IQR]) age was 57 (47, 70) years, 65% of them were males, and 45% had GI symptoms (e.g. abdominal pain, diarrhea, vomiting) on hospital presentation (Table 1). The median (IQR) Sequential Organ Failure Assessment (SOFA) Score upon admission to the ICU was 5 (4, 7.5), and 128 (91%) required mechanical ventilation. A total of 104 patients (74%) developed at least one GI complication.

We stratified the GI complications into four categories: hepatobiliary, hypomotility, bowel ischemia, and other. Among the hepatobiliary complications, transaminitis was the most common (67%). The mean highest values recorded for aspartate aminotransferase (AST) and Alanine Aminotransferase (ALT) were 420.7 U/L and 479.0 U/L respectively, representing a 7.5- and 12-fold increase from the physiological values. Four patients (4%) developed acute acalculous cholecystitis and one patient (1%) developed acute pancreatitis during their ICU stay.

Half of the patients developed hypomotility-related complications of variable severity. Almost all patients with GI complications required nasogastric or orogastric tubes. Forty-six percent of patients had gastric feeding held for at least 24 hours due to high gastric residuals, and 58 (56%) developed an ileus diagnosed clinically and/or radiologically. Four of the patients with severe ileus had clinical and radiologic findings concerning for bowel ischemia and were taken to the operating room on days 11, 14, 15, and 22 of hospitalization, respectively, for an exploratory laparotomy. Two patients were found to have extensive patchy bowel necrosis involving half to two thirds of the total bowel length, despite patent proximal mesenteric vessels on the computed imaging (CT) scan, perhaps suggesting microvessel thrombosis. Intraoperatively, the necrotic bowel had a distinct bright yellow color in contrast to the common finding of purple-black color (Figure 1 in the Supplementary Appendix). Another patient was found to have ischemia without frank necrosis of the terminal ileum. The fourth patient developed liver ischemia and necrosis, and had similar areas of yellow discoloration on the antimesenteric side of the small bowel, without frank transmural necrosis.

Two additional patients were diagnosed with a colonic paralytic ileus, clinically identical to colonic pseudoobstruction (Ogilvie's syndrome) on days 6 and 14 of hospitalization. Figure 2 in the Supplementary Appendix shows an abdominal x-ray of one of these two patients demonstrating significant colonic dilation with cecal wall pneumatosis. On exploratory laparotomy, patchy areas of necrosis of the entire colon were noted; a total colectomy and an end ileostomy were performed. The pathology of the resected bowel showed focal transmural areas of necrosis with acute fibrinopurulent serositis. The overall 14-day patient mortality was 15%. The mortality rate of the subset of patients who required abdominal surgery was as high as 40%.



In this series of critically ill patients with COVID-19, we report a high incidence of hepatobiliary, hypomotility, and ischemic GI complications. Of 141 patients, 58 had ileus, two had an Ogilvie-like syndrome, one had extensive hepatic necrosis, and four had bowel ischemia necessitating emergent surgery and bowel resection. Although these GI complications could be attributed to pharmacologic adverse events and metabolic and electrolyte disturbances occasionally encountered in critically ill patients, SARS-CoV-2-induced small vessel thrombosis or viral enteroneuropathy are two possible hypotheses that warrant further investigation (4, 5). In summary, critically ill COVID-19 patients have a high incidence of GI complications with a subset that progress to bowel ischemia requiring emergent surgical intervention. Front line clinicians should be made aware of these complications and should keep a high index of suspicion for GI symptoms warranting surgical consultation.



#### **REFERENCES**

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### **TABLES**

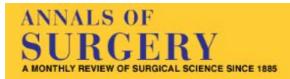
Table 1. Characteristics of patients with severe COVID-19 admitted to the ICU

Characteristics	Patients (n=141)
Age, median (IQR)	57 (47, 70)
Male	92 (65.2%)
BMI, median (IQR)	30.8 (27.2, 35.5)
GI manifestations on admission	
Diarrhea	42 (29.8%)
Nausea/vomiting	31 (22.0%)
Abdominal pain	21 (14.9%)
ICU admission SOFA score, median (IQR)	5 (4, 7.5)
Mechanical ventilation	128 (90.8%)
Patients with at least one GI complication	n=104 (73.8%)
GI manifestations during admission*	
Abdominal pain	15 (14.4%)
Abdominal distention	39 (37.5%)
Diarrhea	30 (28.8%)
Constipation	41 (39.4%)
Nausea	18 (17.3%)
Vomiting	44 (42.3%)
Enterostomies and drains*	(.2.070)
Nasogastric/Orogastric tube	100 (96.2%)
Rectal tube	84 (80.8%)
Gastrostomy tube	5 (4.8%)
Ostomy	2 (1.9%)
Hepatobiliary complications*	2 (2.576)
Transaminitis	70 (67.3%)
Highest AST, mean (SD)	420.7 (942.0)
Highest ALT, mean (SD)	479.0 (1712.8)
Acute cholecystitis	4 (3.8%)
Acute pancreatitis	1 (1.0%)
Hepatic ischemia and necrosis	1 (1.0%)
Hypomotility complications*	1 (1.070)
Gastric feeding intolerance ≥ 24h	48 (46.2%)
lleus (clinical or radiological diagnosis)	58 (55.8%)
Parenteral nutrition	4 (4.8%)
Ogilvie-like syndrome	2 (1.9%)
Bowel ischemia*	5 (3.8%)
Cecum	1 (1.0%)
Small and large intestine	1 (1.0%)
Small intestine	3 (2.9%)
Other GI complications*	44 (40 00)
Gastrointestinal bleeding	11 (10.6%)
Clostridium difficile colitis	4 (3.8%)

Abbreviations – BMI: body mass index, IQR: interquartile range, GI: gastrointestinal, ICU: intensive care unit, SOFA: Sequential Organ Failure Assessment, SD: standard deviation, AST: aspartate aminotransferase, ALT: alanine aminotransferase

<sup>\*</sup> Percentage is of patients with at least one GI complication

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### **FIGURE LEGENDS**

**Supplemental Figure 1.** Diffuse patchy areas of necrosis of the entire small bowel and right colon, involving large and short stretches of the wall. Note the clear demarcation, the round shape, and the antimesenteric location





**Supplemental Figure 2.** Abdominal x-ray of a patient with an Ogilvie-like syndrome showing significant distention of the colon.



# LIST OF SUPPLEMENTAL DIGITAL CONTENT

Supplemental Digital Content 1.TIFF Supplemental Digital Content 2.TIFF



### **ETHICS COMMITTEE APPROVAL**

Institutional review board approval was obtained for this report. Consent for publishing the Accepted for publication in Annals of Surgers unidentifiable patient imaging and operative pictures was obtained.