Association of Digestive Symptoms and Hospitalization in Patients With SARS-CoV-2 Infection

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INTRODUCTION: High rates of concurrent gastrointestinal manifestations have been noted in patients with coronavirus disease 2019 (COVID-19); however, the association between these digestive manifestations and need for hospitalization has not been established.

METHODS: This is a retrospective review of consecutive patients diagnosed with COVID-19. A total of 207 patients were identified; 34.5% of patients noted concurrent gastrointestinal symptoms, with 90% of gastrointestinal symptoms being mild.

RESULTS: In a multivariate regression model controlled for demographics and disease severity, an increased risk of hospitalization was noted in patients with any digestive symptom (adjusted odds ratio 4.84, 95% confidence interval: 1.68–13.94).

DISCUSSION: The presence of digestive symptoms in COVID-19 is associated with a need for hospitalization.

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INTRODUCTION
The current pandemic caused by the severe acute respiratory syndrome coronavirus (SARS-CoV)-2 continues to spread globally, and as of April 13, 2020, more than 1.7 million cases have been reported worldwide (1). Although respiratory manifestations preponderate in patients with SARS-CoV-2 infection (2,3), emerging data suggest a significant prevalence of concurrent gastrointestinal symptomology (4). Our aim was to examine the association between clinical and disease characteristics, including concurrent digestive manifestations, and need for hospitalization in patients with confirmed coronavirus disease 2019 (COVID-19).

METHODS
After expedited approval from our Institutional Review Board, we analyzed retrospectively collected data from consecutive patients with confirmed COVID-19 based on a positive polymerase chain reaction testing at our institution from March 3, 2020, to April 7, 2020. Baseline demographic, clinical, laboratory, and patient-reported symptom data were collected at presentation. Multivariable logistic regression analyses were performed to assess likelihood for hospitalization with digestive symptoms (nausea/vomiting, diarrhea, abdominal pain, and loss of appetite) after adjusting for clinical demographics (age, sex, and race/ethnicity), chronic comorbidities, duration of symptoms, oxygen status, and respiratory symptoms at presentation. Patients with missing covariate data were excluded from the regression model.

RESULTS
Clinical demographics and characteristics of 207 patients with confirmed COVID-19 are listed in Table 1. Of these 207 patients, 60 patients (29.0%) were hospitalized, with 17 patients (8.2%) requiring intensive care unit level of care. To date, there have been 4 COVID-19–related deaths. Overall, a higher prevalence of men, hypertension, and diabetes mellitus were seen in patients who were hospitalized (P < 0.05). Respiratory viral coinfection was found in 14 of 146 (9.1%) tested patients, of whom 2 patients were hospitalized, and 3 patients had digestive symptoms. Concurrent digestive symptoms were noted in more than one-third of all patients, with a higher prevalence observed in those hospitalized to the medical floor and intensive care unit compared with those seen only in the emergency room (Table 2); 90% of all digestive symptoms were characterized as mild in severity. Prevalence of acute renal insufficiency was observed to be higher in patients with digestive symptoms than those without digestive symptoms (9.3% vs 3.1%).

After adjusting for confounders and clinical covariates, patients experiencing any digestive symptoms had a more than 4-fold higher odds for hospitalization (adjusted odds ratio [OR] 4.84, 95% confidence interval [CI]: 1.68–13.94, P < 0.001). Diarrhea was associated with a 7-fold higher likelihood for hospitalization (adjusted OR = 7.58, 95% CI: 2.49–20.02, P < 0.001), and nausea or vomiting had a 4 times higher odds (adjusted OR 4.39, 95% CI: 1.61–11.4, P = 0.005).

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|                          | All patients, N = 207 | Not hospitalized, N = 147 | Hospitalized, N = 60 | Level of hospitalization |
|--------------------------|------------------------|----------------------------|----------------------|--------------------------|
|                          |                        |                            |                      | Medical floor, N = 43    |
| Age (yr)                 | 49 (34–65)             | 43 (31–58)a                 | 62 (43–77)           | 65 (45–77)               |
| Men                      | 104 (50.2)             | 72 (49.0)a                  | 32 (53.3)            | 22 (51.2)               |
| Women                    | 103 (49.8)             | 75 (51.0)a                  | 28 (46.7)            | 21 (48.8)               |
| Race/ethnicity           |                        |                            |                      | Intensive care unit, N = 17 |
| White                    | 87 (42.4)              | 66 (44.9)                   | 21 (36.2)            | 18 (41.9)               |
| Asian                    | 42 (20.5)              | 27 (18.4)                   | 15 (25.9)            | 11 (25.6)               |
| Hispanic                 | 62 (30.2)              | 45 (30.6)                   | 17 (29.3)            | 9 (20.9)                |
| Black                    | 2 (1.0)                | 1 (0.7)                     | 1 (1.7)              | 1 (2.3)                 |
| Other                    | 12 (5.9)               | 8 (5.4)                     | 4 (6.9)              | 4 (9.3)                 |
| Body mass index (kg/m²)  | 26.3 (23.2–31.0)       | 25.4 (23.1–30.8)            | 28.0 (24.0–32.5)     | 27.0 (23.8–31.2)        |
| Current smoker           | 3 (1.6)                | 1 (0.7)                     | 2 (3.5)              | 2 (4.8)                 |
| History of recent travel |                        |                            |                      |                         |
| Domestic                 | 20 (10.1)              | 16 (11.4)                   | 4 (6.8)              | 1 (2.3)                 |
| International            | 20 (10.1)              | 16 (11.4)                   | 4 (6.8)              | 4 (9.3)                 |
| Cruise                   | 6 (3.0)                | 4 (2.9)                     | 2 (3.4)              | 1 (2.3)                 |
| Healthcare worker        | 22 (10.6)              | 16 (10.8)                   | 6 (10.2)             | 3 (7.0)                 |
| Known exposure to COVID-19 | 73 (36.8)             | 52 (37.1)                   | 21 (36.2)            | 14 (33.3)               |
| Medical history          |                        |                            |                      |                         |
| Chronic liver disease    | 5 (2.7)                | 4 (3.1)                     | 1 (1.7)              | 1 (2.3)                 |
| Chronic pulmonary disorder| 42 (20.3)              | 25 (17.0)                   | 17 (28.3)            | 13 (30.2)               |
| Hypertension             | 52 (25.5)              | 30 (20.7)a                  | 22 (37.3)            | 14 (33.3)               |
| Diabetes                 | 33 (16.0)              | 16 (11.0)a                  | 17 (28.3)            | 10 (23.3)               |
| Cardiovascular disease   | 24 (11.7)              | 13 (8.9)                    | 11 (18.3)            | 10 (23.3)               |
| Metabolic syndrome       | 19 (9.2)               | 8 (5.5)a                    | 11 (18.3)            | 8 (18.6)                |
| Chronic kidney disease   | 10 (4.4)               | 2 (1.4)                     | 8 (13.3)             | 7 (16.3)                |
| Medication use           |                        |                            |                      |                         |
| Angiotensin-converting enzyme inhibitors/ angiotensin-receptor blockers | 23 (11.2) | 14 (9.6) | 9 (15.0) | 5 (11.6) |
| Chronic immunosuppression | 7 (3.4)                | 4 (2.7)                     | 3 (5.0)              | 3 (7.0)                 |
| Immunotherapy            | 5 (2.4)                | 3 (2.1)                     | 2 (3.3)              | 1 (2.3)                 |

COVID-19, coronavirus disease 2019; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.
remains unknown. Of viremia or from an alternative pathophysiologic process, digestive symptoms are a surrogate clinical marker for higher levels as COVID-19 progresses (6). Whether digestive symptoms include nausea or vomiting, diarrhea, abdominal pain, or loss of appetite.

Table 2. Clinical presentation of respiratory and gastrointestinal symptoms and laboratory findings at initial evaluation in patients with confirmed SARS-CoV-2 infection

| Symptom                                      | All patients N = 207 | Not hospitalized N = 147 | Hospitalized N = 60 | Level of hospitalization Med. floor N = 43 | Intensive care unit N = 17 |
|----------------------------------------------|----------------------|--------------------------|---------------------|---------------------------------------------|---------------------------|
| Fever                                       | 142 (68.6)           | 92 (62.6)a               | 50 (83.3)           | 36 (83.7)                                   | 14 (82.4)                 |
| Cough                                       | 175 (85.4)           | 118 (80.8)a              | 57 (96.6)           | 41 (95.6)                                   | 16 (94.1)                 |
| Shortness of breath                         | 106 (52.2)           | 58 (39.5)a               | 50 (83.3)           | 34 (79.0)                                   | 16 (94.1)                 |
| Sore throat                                 | 54 (26.2)            | 43 (29.3)                | 11 (18.6)           | 6 (14.3)                                    | 5 (29.4)                  |
| Myalgias                                    | 105 (51.0)           | 68 (46.6)                | 37 (61.7)           | 23 (53.5)                                   | 14 (82.4)                 |
| Duration of respiratory viral symptoms, d  | 5 (3–7)              | 5 (3–7)a                 | 7 (3.5–9)           | 7 (3–9)                                     | 7 (6–8)                   |
| Gastrointestinal symptoms                   |                      |                          |                     |                                             |                           |
| Any gastrointestinal symptomb              | 70 (34.5)            | 34 (23.5)a               | 36 (60)             | 26 (63.1)                                   | 10 (58.2)                 |
| Nausea or vomiting only                     | 22 (10.8)            | 14 (9.6)a                | 8 (13.8)            | 6 (14.6)                                    | 2 (11.8)                  |
| Diarrhea only                               | 22 (10.8)            | 10 (6.9)a                | 12 (20.7)           | 8 (19.5)                                    | 4 (23.5)                  |
| Nausea or vomiting and diarrhea            | 10 (4.9)             | 3 (2.1)                  | 7 (12.1)            | 5 (12.2)                                    | 2 (11.8)                  |
| Abdominal pain                              | 14 (7.1)             | 10 (7.1)                 | 4 (7.0)             | 4 (10.0)                                    | 0                         |
| Duration of gastrointestinal symptoms, d    | 1 (0–4)              | 1 (0–3)                  | 2 (1–4)             | 2 (1–4)                                     | 4 (2–7)                   |
| Laboratory values n = 115                  |                      |                          |                     |                                             |                           |
| White blood cell count (K/µL)               | 5.6 (4.1–7.3)        | 5.8 (4.5–7.2)            | 5.4 (3.9–7.8)       | 5.2 (3.8–8.2)                               | 5.3 (3.9–7.0)             |
| Absolute lymphocyte count (K/µL)           | 0.9 (0.7–1.5)        | 1.1 (0.8–1.7)            | 0.9 (0.6–1.2)       | 0.9 (0.6–1.2)                               | 0.6 (0.4–1.0)             |
| Platelet count (K/µL)                       | 190 (159–241)        | 203 (169–244)            | 182 (153–241)       | 183 (142–241)                               | 181 (157–250)             |
| Serum sodium (mmol/L)                       | 138 (135–141)        | 139 (136–141)a           | 136 (133.5–139)     | 136 (132–139)                               | 136 (134–138)             |
| Serum creatinine (mg/dL)                    | 0.8 (0.6–1.0)        | 0.8 (0.6–0.9)a           | 0.9 (0.7–1.1)       | 0.9 (0.8–1.1)                               | 0.8 (0.5–1.0)             |

SARS-CoV-2; severe acute respiratory syndrome coronavirus 2.

DISCUSSION

We demonstrate that a significant portion of COVID-19 patients have concurrent mild gastrointestinal symptoms and that the presence of these digestive symptoms is associated with a need for hospitalization. The pathogenesis for gastrointestinal involvement related to SARS-CoV-2 is unknown. However, a critical cellular receptor in the SAR-CoV-2 lifecycle, angiotensinconverting enzyme 2, is abundantly expressed throughout the gastrointestinal tract (5) and might play a role in worsening digestive symptoms as COVID-19 progresses (6). Whether digestive symptoms are a surrogate clinical marker for higher levels of viremia or from an alternative pathophysiologic process remains unknown.

There are several limitations to our findings. Because this is a retrospective single institution study, our findings might not be broadly generalizable. In addition, because this series represents our initial experience treating COVID-19, it is unclear whether these results should be viewed on a continuum with changing demographic and clinical information with time. Moreover, because of the short study duration, we were unable to further assess hospitalization outcomes.

In conclusion, while analyzing our initial clinical and demographic data in patients with COVID-19, we identified the presence of gastrointestinal symptoms as a risk factor of higher severity of overall illness and need for hospitalization. With the current focus on streamlining triaging efforts, first responders and frontline providers should consider assessing for digestive symptoms in their initial clinical evaluation and decision making. Larger prospective studies are needed to validate these observations.

CONFLICTS OF INTEREST

Guarantor of the article: Alexander Podboy, MD and George Cholankeril, MD, MS.

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