Characteristics and Outcomes Based on Perceived Illness Severity in SARS-CoV-2

David Snipelisky, MD, Rachel Johnson, MD, Rajnish Prasad, MD, Baqir Lakhani, DO, and Jeffrey Ellington, MD

Objectives: The severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) epidemic is characterized by a global sense of uncertainty, partly driven by the paucity of real-life clinical data. This study assessed whether admission patient characteristics were associated with need for intensive care unit (ICU) care.

Methods: The observational study included consecutive patients admitted to a large community teaching hospital with a diagnosis of SARS-CoV-2 between March 6, 2020 and March 31, 2020. Comparisons were made based on the need for ICU admission.

Results: A total of 156 patients were admitted, 42 of whom (26.9%) required ICU admission and 114 (73.1%) did not. No difference in age (61.9 years vs 60.5 years, \( P = 0.67 \)), race/ethnicity, or comorbidities were noted, except that patients requiring ICU care had lower serum albumin levels and lymphocyte counts and higher liver function tests, white blood cell count, and absolute neutrophil count on admission. The average time from admission to death was similar (10 days in an ICU subset vs 9.2 days in a non-ICU subset, \( P = 0.78 \)), yet patients necessitating ICU care had longer hospital lengths of stay (10.2 vs 5.1 days, \( P = 0.0002 \)). At the time of data extraction, 15 patients in the ICU had died, 7 were discharged from the hospital, and 20 were still admitted while 5 patients died in the non-ICU cohort with 97 discharged and 12 patients admitted.

Conclusions: This is the largest study assessing clinical differences based on the need for ICU admission in inpatients with SARS-CoV-2. It found few major differences in clinical variables between subsets. Among patients admitted to the ICU, outcomes were generally poor.

Key Words: coronavirus disease 2019 (COVID-19), critical care, intensive care, prognosis, severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2)

Key Points
- Significant variability in disease manifestation exists among patients with coronavirus disease 2019.
- Of patients admitted to the hospital with a primary diagnosis of severe acute respiratory syndrome-coronavirus-2 infection, a significant proportion tend to require intensive care unit (ICU)–level care.
- Limited differences in admission variables exist among patients requiring ICU care and those who do not.
- Patients requiring ICU care tend to have poor outcomes.
retrospective cohort of >1500 patients in Italy, which demonstrated the high use of mechanical ventilation, with high mortality rates among patients necessitating admission to intensive care units (ICUs).

Although these data highlight the need to take SARS-CoV-2 seriously, it is also important to understand that the Italian population differs significantly from that of other countries, including the United States, as it has the second oldest population in the world. To date, the largest study in the United States evaluated 24 patients admitted to ICUs at nine different hospitals in the state of Washington and provided us with limited guidance in a more representative population. Considering the scarcity of data in this important patient population, the goal of our study is to expand on the current literature and assess clinical differences based on the need for ICU care among patients admitted to the hospital with a confirmed diagnosis of SARS-CoV-2 in an effort to identify potential prognostic markers.

Methods
This retrospective observational study included consecutive patients admitted to a large teaching community hospital between March 6, 2020 and March 31, 2020 with a laboratory-confirmed diagnosis of COVID-19. All of the patients admitted to our institution with either a confirmed diagnosis of COVID-19 or if classified as a person under investigation (COVID-19 suspected, yet test results pending) were recorded and information maintained as part of our institution’s infection control process, and this list was used for this study’s purposes. Clinical demographics, laboratory analysis, and features of the hospital course were collected by review of the electronic medical record. Patients were stratified into one of two groups based on the need for ICU admission during hospitalization, and comparisons of clinical variables were made to assess for differences among the groups. Patients were excluded if hospitalized for a different etiology than COVID-19 and COVID-19 diagnosed subsequently during the hospitalization. All of the testing for COVID-19 was performed via polymerase chain reaction assays of nasopharyngeal samples as send-out testing to Quest Diagnostics. Other laboratory and diagnostic testing, as well as the treatment strategy, was performed at the discretion of the admitting clinical teams. Patient data were censored at the time of data extraction (April 6, 2020). Electrocardiograms were individually reviewed in a blinded fashion by a board-certified cardiologist, and evidence of ischemia and/or myocarditis was recorded. Clinical specimens for COVID-19 testing were obtained and tests performed per current Centers for Disease Control and Prevention recommendations.

Diagnoses and comorbidities were extracted per review of the electronic medical record and/or admission documentation, including active International Classification of Diseases (ICD) codes. Initial vital signs include those taken on admission to the hospital in the emergency department, and all of the initial laboratory evaluations were performed within 24 hours of admission. ACE inhibitor use was collected if a patient verified the use of one of these agents before admission for any indication. Vasoactive use was defined as the need for intravenous vasoactive medications to support hemodynamics. Code status, including full code, do not attempt resuscitation, or any variance thereof, are routinely discussed with patients/family on admission and documented in the electronic medical record. Any change in code status during the hospitalization also was noted.

Descriptive analyses were used to summarize the data. Results were reported as means and standard deviations. t test and analysis of variance were used to compare data points. No imputations were performed on missing data. Institutional review board approval was obtained before study initiation.

Results
Of 520 consecutive patients admitted with suspected COVID-19 between March 6, 2020 and March 31, 2020, 156 (30%) had positive results on laboratory testing. Two patients were excluded because one patient was admitted for emergent trauma surgery and found to have COVID-19 during the latter part of the hospitalization and another tested positive as part of a transplant donor evaluation. Almost all of the patients were admitted to the hospital as a result of respiratory distress. A total of 42 (26.9%) required admission to the ICU and 114 (73.1%) did not. No differences in patient age (61.9 vs 60.5 years, P = 0.67), race/ethnicity, or basic comorbidities were found between patients admitted to the ICU and those who were not. Most of the patients were full code, and no difference in code status was present between both subsets. Patients admitted to the ICU had a trend toward an increase in weight (99 kg vs 90.7 kg, P = 0.081) and body mass index (33.2 vs 30.9, P = 0.094), yet there was no statistical significance. Admission vital signs were similar, apart from a higher temperature (100.4°F vs 99.7°F, P = 0.018) and lower noninvasive oxygenation saturation on room air (89% vs 94.1%, P < 0.0001) among patients admitted to the ICU. Patients requiring ICU care had lower serum albumin levels (3.4 vs 3.7 g/dL, P = 0.0097), higher aspartate aminotransferase (AST) (66 vs 38 U/L, P = 0.0001) and alanine aminotransferase (ALT) (55 vs 30 U/L, P = 0.001) values, higher white blood cell (8.4 vs 6.3 μL, P = 0.001) and absolute neutrophil (6.9 vs 4.6/mm³, P = 0.0001) counts, and lower absolute lymphocyte counts (0.86 vs 1.1/μL, P = 0.012). In addition, patients admitted to the ICU were more likely to have electrocardiogram (ECG) abnormalities (n = 18, 47.4% vs n = 16, 21.6%; P = 0.010), yet troponin elevation was uncommon. One patient developed clinically significant heart failure with presumed acute reduction in ejection fraction to 10% and a troponin T elevation of 0.30 ng/mL. Patients requiring ICU care also were noted to have higher ferritin levels on admission (1319 vs 720 ng/mL, P = 0.0088). Admission chest imaging, including radiography and computed tomography imaging, demonstrated normal and/or unchanged findings in 26% of patients admitted to the ICU and in 32% of patients admitted to the ICU, respectively. All of the patients had an upper respiratory infection panel performed, and in the non-ICU cohort, there was one patient with concomitant rhinovirus, one with influenza type B, and one with metapneumovirus. No patient in the ICU subset was found to have a second concomitant viral infection.
Table 1. Baseline clinical characteristics on admission to the hospital

|                      | All patients | ICU  | Non-ICU | P   |
|----------------------|--------------|------|---------|-----|
| n                    | 156          | 42   | 114     |     |
| Age, y               | 60.9 ± 17    | 61.9 ± 15.5 | 60.5 ± 17.7 | 0.07 |
| Male sex, n (%)      | 85 (54.5)    | 28 (66.7) | 57 (50) | 0.064 |
| Full code status, n (%) | 141 (90.4) | 39 (92.9) | 102 (89.5) | 0.28 |
| BMI (kg/m²)          | 31.5 ± 7.4   | 32.3 ± 7.7 | 30.9 ± 7.2 | 0.094 |
| Weight (kg)          | 92.9 ± 26    | 99 ± 27 | 90.7 ± 25.4 | 0.081 |
| Ethnicity, n (%)     |              |       |         |     |
| Black/AA             | 63 (40.4)    | 21 (50) | 42 (36.8) |     |
| White                | 64 (41)      | 13 (31) | 51 (44.7) |     |
| Asian                | 6 (3.8)      | 1 (2.4) | 5 (4.4) |     |
| Hispanic             | 16 (10.3)    | 4 (9.5) | 12 (10.5) |     |
| Other/undisclosed     | 4 (2.6)      | 0 | 4 (3.5) |     |
| CAD, n (%)           | 19 (12.2)    | 6 (14.3) | 13 (11.4) | 0.63 |
| HFrEF, n (%)         | 2 (1.3)      | 0 | 2 (1.8) | 0.39 |
| HFrEF, n (%)         | 5 (3.2)      | 0 | 5 (4.4) | 0.17 |
| CKD, n (%)           | 20 (12.8)    | 6 (14.3) | 14 (12.3) | 0.74 |
| COPD, n (%)          | 12 (7.7)     | 5 (11.9) | 7 (6.1) | 0.23 |
| DM, n (%)            | 46 (29.5)    | 12 (28.6) | 34 (29.8) | 0.88 |
| Duration symptoms    | 6 ± 3.9      | 6 ± 3.7 | 6 ± 4 | 0.94 |
| before admission, d  |              |       |         |     |
| Oxygen saturation, % | 92.7 ± 5.3   | 89 ± 8.1 | 94.1 ± 2.9 | 0.0001 |
| HR, bpm              | 89.3 ± 17    | 92.7 ± 19 | 88 ± 16 | 0.13 |
| SBP, mm Hg           | 130 ± 23     | 128 ± 21 | 131 ± 24 | 0.52 |
| DBP, mm Hg           | 77 ± 13      | 75 ± 13 | 78 ± 12 | 0.26 |
| Temperature, °F       | 99.9 ± 1.7   | 100.4 ± 2 | 99.7 ± 1.5 | 0.018 |
| ACEi use, n (%)       | 26 (16.7)    | 5 (11.9) | 22 (19.3) | 0.34 |
| Hemoglobin, g/dL      | 13.1 ± 1.9   | 13.1 ± 1.7 | 13.1 ± 1.9 | 0.68 |
| Platelets, per μL     | 213 ± 73     | 220 ± 79.3 | 210 ± 71.2 | 0.45 |
| Sodium, mEq/L         | 137 ± 3.8    | 137 ± 4 | 138 ± 3.6 | 0.3 |
| Albumin, g/dL         | 3.6 ± 0.46   | 3.4 ± 0.46 | 3.7 ± 0.44 | 0.0097 |
| Creatinine, mg/dL     | 1.43 ± 1.8   | 1.52 ± 1.6 | 1.4 ± 1.9 | 0.7 |
| AST, U/L              | 47 ± 35      | 66 ± 48 | 38 ± 22 | 0.0001 |
| ALT, U/L              | 39 ± 37      | 55 ± 52 | 30 ± 22 | 0.001 |
| WBC, per μL           | 6.9 ± 3.3    | 8.4 ± 4.3 | 6.3 ± 2.6 | 0.0003 |
| Absolute neutrophil count, per mm³ | 5.2 ± 3.1 | 6.9 ± 4 | 4.6 ± 2.3 | 0.0001 |
| Absolute lymphocyte count, per mm³ | 1.04 ± 0.53 | 0.86 ± 0.43 | 1.1 ± 0.55 | 0.012 |
| Troponin T, ng/L      | 0.024 ± 0.07 | 0.041 ± 0.1 | 0.015 ± 0.04 | 0.092 |
| LDH, U/L              | 423 ± 328    | 463 ± 224 | 361 ± 242 | 0.057 |
| Ferritin, ng/mL       | 953 ± 1069   | 1319 ± 1439 | 720 ± 661 | 0.0088 |
| Abnormal ECG (%)§     | 34/112 (30.4) | 18/38 (47.4) | 16/74 (21.6) | 0.01 |

§ECG percentage based on the number of patients who underwent ECG.

Table 2. Clinical variables noted during hospitalization

|                      | All patients | ICU  | Non-ICU | P   |
|----------------------|--------------|------|---------|-----|
| n                    | 156          | 42   | 114     |     |
| Treatments, n (%)    |              |       |         |     |
| Zinc                 | 50 (32.1)    | 22 (52.4) | 28 (24.6) | 0.00085 |
| Hydroxychloroquine   | 51 (32.7)    | 35 (83.3) | 16 (14) | 0.0001 |
| Azithromycin         | 75 (48.1)    | 26 (61.9) | 46 (40.4) | 0.016 |
| Intubated, n (%)     | 38 (24.4)    | 38 (90.5) | — | — |
| Days to intubation   |              |       |         |     |
| from symptom onset   | 6.2 ± 5.3    | 6.2 ± 5.3 | — | — |
| Days admittance to intubation | 2.8 ± 3.1 | 2.8 ± 3.1 | — | — |
| Vasopactive use (n)  | 29 (18.6)    | 29 (69) | — | — |
| Deceased, n%         | 20           | 15 | 5 | <0.0001 |
| Days admittance to death     | 9.8 ± 5.4 | 10 ± 5.9 | 9.2 ± 4.2 | 0.78 |
| Days admittance to discharge | 5.5 ± 4.1 | 10.2 ± 6.4 | 5.1 ± 3.6 | 0.0002 |
| Change in code status (n)  | 14 (9) | 10 (23.8) | 4 (3.5) | <0.0001 |

ICU, intensive care unit. §20 patients remained admitted to the hospital in the ICU subset and 12 in the non-ICU subset at the time of data extraction; therefore, percentages are not displayed. Statistical analysis excludes patients still admitted.
higher white blood cell counts (14.8 vs 6.1×10^6/μL, P = 0.0001) on discharge. Absolute neutrophil counts were similar among both groups. Table 4 includes laboratory analyses among both patient subsets in routine laboratory evaluations collected during nonacute encounters within 6 months of admission and demonstrates no significant differences between the subsets.

**Discussion**

This single-center, retrospective observational study assessed clinical characteristics and differences among patients admitted to the hospital with COVID-19 requiring ICU care and those who did not. The study included all of the patients admitted to our facility who were confirmed to have COVID-19 by laboratory testing during the defined study period. Our results demonstrate few differences in patient characteristics between patient subsets, with relatively young age and limited comorbidities common. It also illustrates an extremely high need for mechanical ventilation among patients necessitating ICU level care, as well as worse outcomes in this population.

A significant proportion of patients in this study required ICU care during hospitalization for COVID-19 treatment, almost all of whom required mechanical ventilatory support. Furthermore, patients requiring ICU care were relatively young and without a high burden of comorbidities. These findings are similar to those by Grasselli et al and Bharaju et al, yet our observations reveal few clinical demographic differences between patients necessitating ICU-level care and those who did not.2,4 The COVID-19 pandemic has been unpredictable and our findings demonstrate the potential ability of the virus to significantly affect everyone rather than only older patients with significant comorbidities as was previously believed.1 Our study also emphasizes the fact that ICU admission by itself serves as a poor prognostic indicator and should be considered in decision making, particularly in the current pandemic, with the lack of basic medical resources. Interestingly, patients admitted to the ICU were more likely to reverse code status from full code, although this occurred only in a minority of patients. In addition, African American patients were more likely to be admitted to the ICU than any other racial group, perhaps adding evidence that minority groups are disproportionately affected by COVID-19. This observation underscores the need for additional research, in both the spectrum of COVID-19 and other disease processes, to further understand this relationship and, more important, how to prevent it from occurring.

Considering that this virus binds to the ACE2 receptor, which is present in myocardial tissue, the data have suggested a high propensity for cardiac involvement among patients affected by COVID-19.10 Surprisingly, among patients whose serum troponin levels were obtained, almost none had a significant elevation, and troponin levels were relatively unremarkable among both ICU and non-ICU patients, although ECG abnormalities were more prevalent in patients requiring ICU care.

Elevation in liver function tests was prevalent among our population, and patients admitted to the ICU had higher overall levels of both AST and ALT. Although data have demonstrated the presence of mild liver dysfunction in patients with COVID-19, our findings suggest that more significant elevations in liver function tests may be associated with worse outcomes, whether this is a result of multiorgan dysfunction from the systemic inflammatory response or direct impact from the virus itself.7 As has been demonstrated in other non-COVID-19 populations, lower serum albumin levels may be a poor prognostic indicator because patients with lower levels tended to require ICU admission.13 Patients in the ICU also had higher white blood cell counts on discharge, which may be another marker of a heightened and possibly prolonged systemic inflammatory reaction.

Our results demonstrate that the presence of lymphopenia was almost universal among patients with confirmed SARS-CoV-2 infection, and a higher degree of lymphopenia was noted

### Table 3. Laboratory evaluations at hospital discharge

|                      | All patients | ICU          | Non-ICU       | P     |
|----------------------|--------------|--------------|---------------|-------|
| n                    | 156          | 42           | 114           |       |
| Hemoglobin, g/dL     | 11.7 ± 2.2   | 10.5 ± 2.5   | 11.9 ± 2.1    | 0.0087|
| Platelets, per μL    | 264 ± 105    | 280 ± 139    | 260 ± 96      | 0.46  |
| Sodium, mEq/L        | 140 ± 3.8    | 141 ± 5.6    | 139 ± 3.1     | 0.02  |
| Albumin, g/dL        | 3.2 ± 0.52   | 2.7 ± 0.5    | 3.3 ± 0.43    | 0.0001|
| Creatinine, mg/dL    | 1.23 ± 1.6   | 1.52 ± 1.8   | 1.17 ± 1.6    | 0.39  |
| AST, u/L             | 46 ± 30      | 70 ± 34      | 37 ± 23       | 0.0003|
| ALT, u/L             | 47 ± 41      | 68 ± 64      | 39 ± 30       | 0.025 |
| WBC, per μL          | 7.8 ± 6.5    | 14.8 ± 11.7  | 6.1 ± 2.9     | 0.0001|
| Absolute neutrophil count, per mm^3 | 5.56 ± 6.2 | 12.6 ± 10.4 | 3.7 ± 2.1 | 0.0001 |
| Absolute lymphocyte count, per mm^3 | 1.41 ± 0.81 | 1.19 ± 0.95 | 1.47 ± 0.76 | 0.21   |

*ALT, alanine aminotransferase; AST, aspartate aminotransferase; ICU, intensive care unit; WBC, white blood cell count.*

### Table 4. Nonacute laboratory evaluations within 6 months of admission

|                      | All patients | ICU | Non-ICU | P     |
|----------------------|--------------|-----|---------|-------|
| n                    | 156          | 42  | 114     |       |
| Hemoglobin, g/dL     | 12.5 ± 2.1   | 12.6 ± 1.4 | 12.4 ± 2.3 | 0.71  |
| Platelets, per μL    | 229 ± 74     | 253 ± 84 | 219 ± 71  | 0.22  |
| Sodium, mEq/L        | 140 ± 3.7    | 140 ± 3 | 140.2 ± 4 | 0.81  |
| Albumin, g/dL        | 4.1 ± 0.48   | 4.1 ± 0.44 | 4.2 ± 0.5 | 0.62  |
| Creatinine, mg/dL    | 1.3 ± 1.43   | 1.51 ± 2.3 | 1.26 ± 1.1 | 0.61  |
| AST, u/L             | 21 ± 6       | 21 ± 5.9 | 21 ± 6   | 0.86  |
| ALT, u/L             | 20 ± 7       | 20 ± 6  | 20 ± 7   | 0.9   |
| WBC, per μL          | 6.7 ± 1.9    | 6.9 ± 2.3 | 6.6 ± 1.7 | 0.68  |

*ALT, alanine aminotransferase; AST, aspartate aminotransferase; ICU, intensive care unit; WBC, white blood cell count.*

*a51/101 (50.5%) of patients had nonacute laboratory values within 6 months before admission, 12/28 (42.9%) in ICU, and 39/73 (53.4%) in non-ICU cohorts.*
among patients necessitating ICU care, which may be reflective of worse disease severity. Lymphocytes express the ACE2 receptor, and a higher degree of lymphopenia may be a result of more widespread viral activity in more severely affected patients. Interestingly, patients necessitating ICU care were noted to have markedly higher ferritin levels, which supports this finding. Further studies are needed to better understand this relationship. In addition, despite at least some degree of hypoxia and fever among our population, particularly considering the reason for admission in almost all of the patients was respiratory distress, patients generally did not mount a high heart rate response as would have been expected. This may be reflective of somewhat of a Faget sign, in which certain infectious processes do not result in expected increases in heart rate with higher temperature, and this observation highlights the atypical nature of SARS-CoV-2.

Numerous study limitations exist. This was a single-center study and therefore likely not representative of all patients with COVID-19. It was retrospective in nature and thus maintains the biases involved with such a study design. Decisions on timing and need for ICU-level care may vary based on physician-specific practice, which can sometimes be subjective in nature, and ultimately affect outcomes. We contend that this is representative of real-world practice, however. No institution-specific criteria were used in deciding timing on ICU transfer, yet this likely also represents real-world practice, particularly in the setting of uncertainty in the context of a novel virus and paucity of formal clinical guidelines. Furthermore, clinical demographic variables were obtained retrospectively by review of the electronic medical record and may not be all-inclusive. Although these limitations exist, this is the most comprehensive study assessing patients with COVID-19 requiring ICU care in the United States.

This is one of the largest studies to date assessing clinical differences among patients admitted to the hospital with confirmed COVID-19 based on the need for ICU care. Our results illustrate that few patient-specific differences exist among both subsets, and patients admitted to the hospital are generally younger with few comorbidities than previously reported. Most patients admitted to the ICU required mechanical ventilation and outcomes were generally poor. This study also highlights leukopenia, liver dysfunction, ferritin, and hypoalbuminemia as potential markers for disease severity, while troponin elevation was uncommon. These results give further insight into the nature of SARS-CoV-2 and potential clinical implications, particularly in the context of the ongoing epidemic and resultant global response.

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