Supplementary appendix

Data collection

Data was collected manually from Electronic Medical Records (Epic Systems software, Verona, WI). Data included demographics, comorbidities (total number of comorbidities analyzed as a continuous variable), symptoms, vital signs, laboratory values, and radiographic findings on presentation. Additionally, transfers within critical care unit service and medical floors and vice versa, impatient medications (including vasopressors, antibiotics, antiviral therapies, and immunomodulators), supportive measures (including invasive mechanical ventilation and new-onset kidney replacement therapy), and outcomes (including the length of stay, discharge, and mortality) were collected. Presenting vital signs were abstracted from Emergency Department records, and these included lowest oxygen saturation, body temperature, heart rate, blood pressure, and respiratory rate. Initial laboratory testing was defined as the first test results available, usually within 24 hours of admission. Laboratory values included complete blood count, complete metabolic panel, and inflammatory markers previously reported, including d-dimer, ferritin, C-reactive protein, lactate dehydrogenase, creatinine kinase, triglycerides, high-sensitivity troponin, brain natriuretic peptide. Radiographic findings included results from the first chest radiograph obtained during the hospitalization. The final radiology report was abstracted and categorized into mutually exclusive categories of no parenchymal findings ("no acute process"), unilateral infiltrate, bilateral infiltrates, and diffuse infiltrates (lung infiltrates >50%).

Interrater agreement and reliability

A 10% random sample was re-abstracted to ascertain agreement and monitor calibration. We calculated a Cohen's kappa for each categorical variable and intraclass correlation

coefficient for continuous variables collected via chart review. The mean (SD) Cohen's kappa for categorical variables was 0.85 (0.15), with a percentage agreement of 94%, indicating a strong level of interrater agreement [1]. The mean intraclass correlation coefficient for continuous variables was 0.94 (0.08), indicating excellent interrater reliability [2].

Missing values

Litte's missing completely at random (MCAR) test was performed to determine how to handle missing data. The Chi-square for the Little's MCAR test was 1550.641, with a significance of .997, indicating that the values are likely missing completely at random [3]. This allowed us to perform multiple imputations for missing values with rates between 6% and 30%. In its standard implementation, multiple imputation provides valid inference when data are missing at random [4]. Pairwise deletion was implemented for missing values with rates of 5% or less [5]. Of 313 patients, 296 (94.5%) had at least one missing value. Only 16 variables presented missing values. In the entire dataset, 6,204 (86.2%) values had complete data and 995 (13.8%) values were incomplete. Missing values with rates of 31% or more were excluded for any group difference or correlation analyses (Table 1).

Table 1. Variable summary

	Missing	
	N	**Percent**
Interleukin-6	247	78.90%
Triglycerides	217	69.30%
Brain natriuretic peptide	167	53.40%
High-sensitivity troponin	82	26.20%

Creatinine kinase	81	25.90%
Lactic acid	53	16.90%
Lactate dehydrogenase	34	10.90%
C-reactive protein	29	9.30%
D-dimer	27	8.60%
Procalcitonin	23	7.30%
Smoking status	6	1.90%
Total bilirubin	1	0.30%
Alkaline phosphatase	1	0.30%
Aspartate aminotransferase	1	0.30%
Alaline aminotransferase	1	0.30%

Non-proportionality test based on Shoenfeld (partial) residuals

A non-proportionality test based on the Schoenfeld residuals (partial residuals in SPSS) was performed to test the proportionality of all the significant prognostic factors in the multivariate survival analysis and to identify time-dependent prognostic factors. The Schoenfeld residuals for all the covariates (significant prognostic factors in the univariable and multivariable survival analysis) were obtained by running a Cox PH regression model and saved as new variables in the working dataset. After deleting censored observations, a variable containing the ranked order of overall survival time was created. Then, a scatter plot was built for each variable (residuals [y] vs. time [x]). Schoenfeld residuals are independent of time. A plot that shows a non-random pattern against time is evidence of a violation of the PH assumption. Finally, the proportionality assumption for each variable was tested for a non-zero slope in a generalized linear regression of the scaled Schoenfeld

residuals on functions of time. The P-value used for the non-proportionality test was the P-value used in the generalized linear regression model. A P-value <0.05 indicated a violation of the proportionality assumption. Variables that violated the proportionality assumption were included in a model with interaction between time (T_COV in SPSS) and the problem variable to adjust for its time-dependent effect. Variables that violated the proportionality assumption in our model included long-term care facility residence, systolic blood pressure, qSOFA score, and blood urea nitrogen.

Study Definitions

COVID-19 illness severity was defined according to NIH guidelines [6]. Sepsis and septic shock were defined according to the 2016 Third International Consensus Definition for Sepsis and Septic Shock [7]. Acute kidney injury was diagnosed according to the KDIGO clinical practice guidelines [8], and acute respiratory distress syndrome (ARDS) was diagnosed according to the Berlin Definition [9]. The American College of Cardiology cut-off for high-sensitivity troponin was used to define acute cardiac injury [10]. Rhabdomyolysis was established as an elevation of creatinine kinase concentration five times the upper limit of the normal reference range [11]. Other definitions include: long-term care facilities groups board and care homes, assisted living facilities, nursing homes, and continuing care retirement communities; neurocognitive impairment as any type of dementia, Parkinson's disease with cognitive impairment, intellectual disability, or cerebral palsy; altered mental status as any alteration in alertness, orientation or level of consciousness; immunosuppression as patients on daily dose ≥20 mg of prednisone or equivalent, active chemotherapy, immunotherapy, immunomodulators (immunosuppressants), or diagnosed with hematological neoplasia.

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