

# Respiratory involvement parameters in hospitalized COVID-19 patients and their association with mortality and length of stay

Eric Lam DO<sup>1</sup>, Sandra Gomez Paz MD<sup>2</sup>, Dominique Goddard-Harte MD<sup>1</sup>, Yosif N. Pak DO<sup>3</sup>,  
Joshua Fogel PhD<sup>4</sup>, Sofia Rubinstein MD<sup>2</sup>

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**Introduction/Background:** Patients with Coronavirus Disease 2019 (COVID-19) present with a spectrum of respiratory symptoms. There are no studies describing respiratory system involvement adjusted for other organ systems, oxygen saturation nadir, hospitalization days until respiratory involvement, proportion of days of respiratory system involvement, and persistent respiratory involvement at discharge in COVID-19 patients. We studied these parameters in COVID-19 patients that received respiratory therapy interventions and their association with mortality and length of stay (LOS).

**Methods:** A single-center cross-sectional retrospective study of 738 COVID-19 patients with respiratory involvement at a hospital in the New York metropolitan area.

**Results:** COVID-19 patients with respiratory involvement had increased mortality with oxygen requirement of  $\text{FiO}_2 > 55\%$  (OR:39.02, 95% CI:1.59-960.51,  $P < 0.05$ ) and mechanical ventilation (OR:236.64, 95% CI:8.24-6798.93,  $P < 0.01$ ). Respiratory system involvement adjusted for other organ system involvement was associated with increased mortality (OR:1.60, 95% CI:1.20, 2.14,  $P < 0.01$ ) and LOS (B = 0.02, SE = 0.01,  $P < 0.01$ ). Oxygen saturation nadir of 70%-89% was significantly associated with increased LOS (B = 0.07, SE = 0.03,  $P < 0.05$ ), whereas oxygen saturation nadir of <70% was associated with increased mortality (OR:12.95, 95% CI:2.72-61.61,  $P < 0.01$ ). An increased proportion of days in hospital with respiratory system involvement was associated with decreased mortality (OR:0.004, 95% CI:<0.001-0.06,  $P < 0.001$ ) and increased LOS (B = 0.90, SE = 0.07,  $P < 0.001$ ). Respiratory involvement on days 4-7 was associated with decreased mortality (OR:0.02, 95% CI:<0.003-0.17,  $P < 0.001$ ), and respiratory involvement on day >1 was associated with increased LOS. Respiratory involvement persistent at discharge was associated with increased mortality (OR:56.82, 95% CI:18.51-174.43,  $P < 0.001$ ).

**Conclusions:** Among all respiratory parameters, high oxygen requirements and low oxygen saturation nadir are the most predictive of COVID-19 prognosis.

**Key Words:** COVID-19; SARS-CoV-2; mortality; length of stay; respiratory system

## INTRODUCTION

The Coronavirus Disease 2019 (COVID-19) caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) has a presentation spectrum ranging from asymptomatic infection to severe disease [1, 2]. COVID-19 is a systemic disease affecting multiple organ systems [3], but primarily presents as pneumonia that affects the respiratory system [1, 4]. Respiratory failure and acute respiratory distress syndrome (ARDS) are the major complications in severe and critical COVID-19 patients, who often require intensive care unit (ICU) care and invasive mechanical ventilation [2, 5].

The severity of respiratory involvement in COVID-19 is mainly measured by clinical characteristics such as oxygen saturation, supplemental oxygen requirement, and the need for invasive mechanical ventilation [2, 5, 6]. Low admission oxygen saturation and the requirement of mechanical ventilation during hospitalization are associated with worse prognosis and mortality in COVID-19 patients [1, 2, 5, 6]. To our knowledge, there are no reports investigating COVID-19 respiratory system involvement and its association with mortality after adjusting for other organ systems

involvement [3]. During COVID-19 hospitalization, oxygen saturation nadir and on-admission are important parameters for measuring acute respiratory failure. In fact, seeing as acute respiratory failure is the most common in-patient complication in COVID-19 [7], it is surprising to note that no studies that have investigated oxygen saturation nadir during hospitalization and its association with COVID-19 mortality.

The course of respiratory involvement in COVID-19 patients is described as the development of dyspnea on days 4-10 after the initial onset of symptoms which rapidly progresses to ARDS on days 8-14 in severe cases [4, 8, 9]. Although prior studies have reported rapid progression to ARDS after hospitalization in critical COVID-19 patients [10], data on in-hospital disease progression in noncritical COVID-19 patients are lacking. No studies have investigated the number of days of hospitalization until respiratory involvement, proportion of days with respiratory involvement during hospital stay, and persistent respiratory involvement at discharge in COVID-19 patients. Investigation of these parameters is important to assess the prognosis of both critical and non-critical COVID-19 hospitalized patients. We studied these respiratory

<sup>1</sup>Department of Medicine, Nassau University Medical Center, East Meadow, NY, USA

<sup>2</sup>Division of Nephrology & Hypertension, Department of Medicine, Nassau University Medical Center, East Meadow, NY, USA

<sup>3</sup>Department of Medicine, Albany Medical Center, Albany, NY, USA

<sup>4</sup>Department of Business Management, Brooklyn College, Brooklyn, NY, USA

Correspondence: Sofia Rubinstein, Nassau University Medical Center, Division of Nephrology and Hypertension, 2201 Hempstead Turnpike, Box 49, East Meadow, NY 11554, USA, Fax: 516-572-0082, E-mail: [rubinst@numc.edu](mailto:rubinst@numc.edu)

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parameters in COVID-19 patients with respiratory involvement and their association with mortality and LOS.

## METHODS

### Settings and participants

The study was ethically conducted and approved by the local Institutional Review Board on 15 May 2020. Patients signed a waiver for informed consent was because of the retrospective nature of the study. This was a single-center retrospective study of 738 consecutive patients with laboratory-confirmed COVID-19 (positive SARS-CoV-2 real-time PCR from nasopharyngeal swabs) with respiratory involvement in a tertiary-care public hospital in the New York metropolitan area from 1 March 2020 through 15 May 2020. All eligible patients were included in the study to avoid potential bias. Respiratory involvement was defined as any new requirement of supplemental oxygenation from baseline or nadir oxygen saturation <92%. All patients had completed their hospital course with either discharge from the hospital or physician-called time of death.

### Variables

Demographic variables included age (years), sex (male/female), race/ethnicity (Caucasian, African American, Hispanic, East Asian, Southeast Asian (e.g., Indian, Pakistani, and Thai), or other), and insurance status (private, uninsured/emergency Medicaid, regular Medicaid, or Medicare). The comorbidities studied were tobacco use status (never, former, current, or unknown), vaping status (never, current, or unknown), obesity (body mass index >30 kg/m<sup>2</sup>), and Charlson Comorbidity Index (CCI) [11]. Disease severity was measured using the quick Sequential Organ Failure Assessment (qSOFA) [12], ICU level of care during hospitalization (no/yes), intubation during admission (no/yes), and maximum oxygen requirement during hospitalization (none, low fraction of inspired oxygen (FiO<sub>2</sub>) ≤55%, high FiO<sub>2</sub> >55%, or invasive mechanical ventilation). ICU level of care was defined as either the administration of vasopressor, requirement of FiO<sub>2</sub> >55%, or transfer of the patient to one of the ICUs in the medical center at any time during hospitalization. Low FiO<sub>2</sub> ≤55% and high FiO<sub>2</sub> >55% referred to any modality of noninvasive mechanical ventilation: low FiO<sub>2</sub> included nasal cannula and simple face mask, whereas high FiO<sub>2</sub> included non-rebreather mask, high flow device, and bilevel positive airway pressure ventilation. Treatment management variables included the use or nonuse of vasopressors (e.g., norepinephrine, vasopressin, dobutamine, epinephrine, or midodrine), antibiotics, nonsteroidal anti-inflammatory drugs (NSAIDs), angiotensin-converting enzyme inhibitors or angiotensin receptor blocker, antivirals (remdesivir), anti-malarials (hydroxychloroquine and/or chloroquine), steroids, convalescent plasma from donors with prior COVID-19 infection, interleukin-6 inhibitor (IL-6; tocilizumab), and anticoagulant (e.g., heparin, enoxaparin, apixaban, and warfarin).

Eight organ systems were studied: respiratory, cardiovascular, renal, hepatic, hematologic, endocrine, neurological, and musculoskeletal systems. The number of organ systems involved ranged from 1 to 8. Respiratory system involvement was defined as any new requirement of supplemental oxygenation from baseline or nadir oxygen saturation <92% during hospitalization. Cardiovascular involvement was any new troponin elevation >0.04 ng/mL, any new heart failure, acute or chronic heart failure, new or uncontrolled atrial fibrillation, supraventricular tachycardia, new atrioventricular block, new ventricular tachycardia, or any new inotrope or vasopressor use. Renal involvement was defined as either an increase in serum creatinine level >0.3 mg/dL or 1.5 time increase from baseline, defined as the AKIN criteria [13]. Liver involvement was defined as elevated serum alanine aminotransferase more than 1.5 times the normal limit (>60 IU/L) or abnormal total serum bilirubin >1.1 mg/dL. Hematologic involvement was defined as a new abnormal count of any one of the four cell lines from the patient's baseline: white blood cell count <4×10<sup>9</sup>/L or >11×10<sup>9</sup>/L, absolute neutrophil count <1.8×10<sup>9</sup>/L or >7×10<sup>9</sup>/L, hemoglobin count <9.2 g/dL, or platelet count <110×10<sup>9</sup>/L. Endocrine involvement was defined as any blood glucose level <60 mg/dL or >140 mg/dL or any new or higher insulin

administration requirement from the baseline. Neurological involvement was defined as any decrease in the Glasgow Coma Scale [14] or change in mental status from baseline, any new onset of seizure, or any new transient ischemic attack or new cerebrovascular accident. Musculoskeletal involvement was defined as creatine kinase values >1000 units/L.

Further respiratory status characteristics were studied. Oxygen saturation on admission and nadir oxygen saturation during hospitalization were classified into one of three groups (SpO<sub>2</sub> 90%–100%, 70%–89%, or <70%). Respiratory proportion days involved was the proportion of hospital days with respiratory involvement (range 0–1) and was calculated using the number of days with respiratory involvement divided by total hospitalization days. Days to respiratory involvement (day 1, day 2, day 3, day 4–7, or >7 days) was the first hospital day with respiratory involvement, where admission day was hospital day 1. Persistent respiratory involvement at discharge was defined as any respiratory involvement (no/yes) at discharge or death.

The outcome variables were mortality (no/yes) and LOS (days).

### Statistical analysis

Descriptive statistics consisted of mean and standard deviation for the continuous variables and frequency and percentage for the categorical variables. Two models were used to analyze the outcome variables of mortality and LOS. Univariate analyses were used for Model 1 that considered demographic, comorbidity, disease severity, and treatment management variables. A multivariate analysis was used for Model 2 that included all the significant variables from the univariate analyses in Model 1 and added respiratory variables. Mortality was analyzed using logistic regression. LOS was analyzed using linear regression. Logarithmic transformations were performed for the skewed variables. All *P* values were two-sided. Data analyses were conducted using IBM SPSS Statistics version 26 (IBM SPSS Statistics for Windows. Version 26. Armonk, NY: IBM Corporation; 2019).

## RESULTS

The sample characteristics of the 738 COVID-19 patients with respiratory involvement are shown in Table 1. The mean age was above 60 years, more than one-third were female, and almost two-thirds were those either African American or Hispanic. Slightly more than one-fifth of the patients had private insurance, more than half never smoked or vaped, and more than one-third were obese. The mean CCI was almost 3, while mean qSOFA on admission was 1.5. More than half the patients required ICU level of care during hospitalization. On admission, only a small percentage of patients required intubation and mechanical ventilation, and a quarter were intubated during the hospital course. Almost all patients received antibiotic treatment and one-third received steroids. There was a mean of four organ systems involved. More than two-thirds had oxygen saturation of 90%–100% on admission, whereas more than half had an oxygen saturation nadir of 70%–89% during hospitalization. The respiratory proportion days involved was 0.7 (average of 70% total hospitalization days with respiratory involvement). In our cohort population, three-quarters had respiratory involvement on the admission day (day 1), and more than half had respiratory involvement at discharge (either alive or dead). Mortality occurred in one-third of the patient sample and the mean LOS was 10.6 days.

The results of the logistic regression analyses for mortality are shown in Table 2 and Figure 1. In the univariate analyses shown in Model 1, increased age, insurance of regular medicare and medicaid, unknown tobacco use, unknown vaping use, increased CCI, increased qSOFA, ICU care level, intubation at admission, oxygen requirement during hospitalization with high FiO<sub>2</sub> and ventilation, vasopressor, antiviral, steroid, interleukin inhibitor, and increased number of organs involved were each significantly associated with increased odds of mortality. Hispanic race/ethnicity and current tobacco use were each significantly associated with decreased odds for mortality. In the multivariate analysis shown in Model 2, increased age, oxygen requirement during hospitalization with high FiO<sub>2</sub> and ventilation, vasopressor, increased number of organs involved, oxygen saturation nadir <70%, and persistent

**TABLE 1**  
Sample characteristics of 738 COVID-19 patients

Variables	M (SD) or Frequency (Percent)
<b>Demographics</b>	
Age, years (mean)	60.5 (16.28)
Sex (female)	286 (38.8)
Race/ethnicity	
Caucasian	192 (26.0)
African-American	180 (24.4)
Hispanic	312 (42.3)
East Asian	24 (3.3)
Southeast Asian	15 (2.0)
Other	15 (2.0)
Insurance	
Private	160 (21.7)
Uninsured/Emergency Medicaid	161 (21.8)
Regular Medicaid	269 (36.4)
Medicare	148 (20.1)
<b>Comorbidities</b>	
Tobacco use	
Never	470 (63.7)
Former	70 (9.5)
Current	23 (3.1)
Unknown	175 (23.7)
Vaping	
Never	444 (60.2)
Current	0 (0.0)
Unknown	294 (39.8)
Obese (yes)	273 (37.0)
CCI (mean)	2.9 (2.42)
<b>Disease severity</b>	
qSOFA (mean)	1.5 (0.63)
ICU (yes)	383 (51.9)
Intubation admission (yes)	44 (6.0)
Oxygen requirement hospitalization	
None	83 (11.2)
Low FiO <sub>2</sub> ( $\leq$ 55%)	274 (37.1)
High FiO <sub>2</sub> ( $>$ 55%)	194 (26.3)
Invasive mechanical ventilation	187 (25.3)
<b>Treatment management</b>	
Vasopressor (yes)	123 (16.7)
Antibiotic (yes)	706 (95.7)
NSAID (yes)	164 (22.2)
ACEi/ARBs (yes)	85 (11.5)
Antiviral (yes)	16 (2.2)
Antimalarial (yes)	620 (84.0)
Steroid (yes)	245 (33.2)
Convalescent plasma (yes)	53 (7.2)
Interleukin inhibitor (yes)	84 (11.4)
Anticoagulant (yes)	149 (20.2)
<b>Organ involvement</b>	
Respiratory plus other organ systems (mean)	4.0 (1.84)
<b>Respiratory involvement</b>	
Oxygen saturation admission	
90–100	502 (68.0)
70–89	212 (28.7)
$<$ 70	24 (3.3)
Oxygen saturation nadir	
90–100	284 (38.5)
70–89	376 (50.9)
$<$ 70	78 (10.6)
Respiratory proportion days involved (mean)	0.7 (0.20)
Days to respiratory involvement	
1	555 (75.2)
2	87 (11.8)
3	34 (4.6)
4–7	44 (6.0)
$>$ 7	18 (2.4)

**TABLE 1 (Continued)**  
Sample characteristics of 738 COVID-19 patients

Variables	M (SD) or Frequency (Percent)
Respiratory persistent involvement at discharge (yes)	400 (54.2)
<b>Outcomes</b>	
Mortality (yes)	249 (33.7)
Length of stay (days) (mean)	10.6 (11.07)

*Note: M = mean, SD = standard deviation, CCI = Charlson Comorbidity Index, qSOFA = quick sepsis related organ failure assessment, ICU = intensive care unit, FiO<sub>2</sub> = fraction of inspired oxygen, NSAID = nonsteroidal anti-inflammatory drug, ACEi = angiotensin-converting-enzyme inhibitors, ARB = angiotensin II receptor blockers. Respiratory plus other organ systems is the number of organ systems involved. Oxygen saturation admission, oxygen saturation nadir, and days to respiratory involvement proportion days were skewed and still skewed even after logarithmic transformation; categorical variables were used instead of continuous variables.*

respiratory involvement at discharge were significantly associated with increased odds for mortality. Current tobacco use, increased respiratory proportion days involved, and 4–7 days to respiratory involvement were significantly associated with decreased odds for mortality.

The linear regression analyses for LOS are shown in Table 3. In the univariate analyses shown in Model 1, ICU care level, oxygen requirement during hospitalization with low FiO<sub>2</sub>, high FiO<sub>2</sub> and ventilation, vasopressor, antibiotic, NSAID, antiviral, antimalarial, steroid, convalescent plasma, interleukin inhibitor, anticoagulant, and increased number of organs involved were each significantly associated with increased LOS. Female sex and East Asian race/ethnicity was significantly associated with decreased LOS. In the multivariate analysis shown in Model 2, ICU care level, antibiotic, NSAID, steroid, convalescent plasma, interleukin inhibitor, anticoagulant, increased number of organs involved, oxygen saturation nadir 70%–89%, increased respiratory proportion days involved, and all categories of days to respiratory involvement were each significantly associated with increased LOS. Persistent respiratory involvement at discharge was significantly associated with decreased LOS.

## DISCUSSION

We found that increased age, FiO<sub>2</sub>  $>$ 55%, mechanical ventilation, vasopressor use, increased number of organ systems involved, oxygen saturation nadir of  $<$ 70%, and persistent respiratory involvement at discharge were each associated with increased odds for mortality. Current tobacco smoking, increased respiratory involvement proportion days, increased respiratory involvement proportion days, and respiratory involvement starting on days 4–7 were associated with decreased odds for mortality. Sex, race/ethnicity, and insurance status, after multivariate adjustment showed no association with mortality. ICU care level, use of antibiotics, NSAIDs, steroids, convalescent plasma, IL6 inhibitors, and anticoagulants were associated with increased LOS. An increased number of organ systems involved, oxygen saturation nadir of 70%–89% during hospital stay, and increased respiratory involvement proportion days were each associated with increased LOS. Respiratory involvement starting on day 2, day 3, days 4–7, and days  $>$ 7 were each associated with increased LOS as compared with respiratory involvement on day of admission. Persistent respiratory involvement at discharge was associated with decreased LOS. FiO<sub>2</sub>  $>$ 55%, mechanical ventilation, and oxygen saturation nadir of  $<$ 70% were each not significantly associated with LOS.

We found that respiratory involvement adjusted for all other organ system involvement was significantly associated with increased odds of mortality and LOS. COVID-19 patients with significant respiratory involvement often present with multiple organ systems involvement [1, 3, 4]. Respiratory parameters such as low admission oxygen saturation, ARDS, and mechanical ventilation are associated with increased

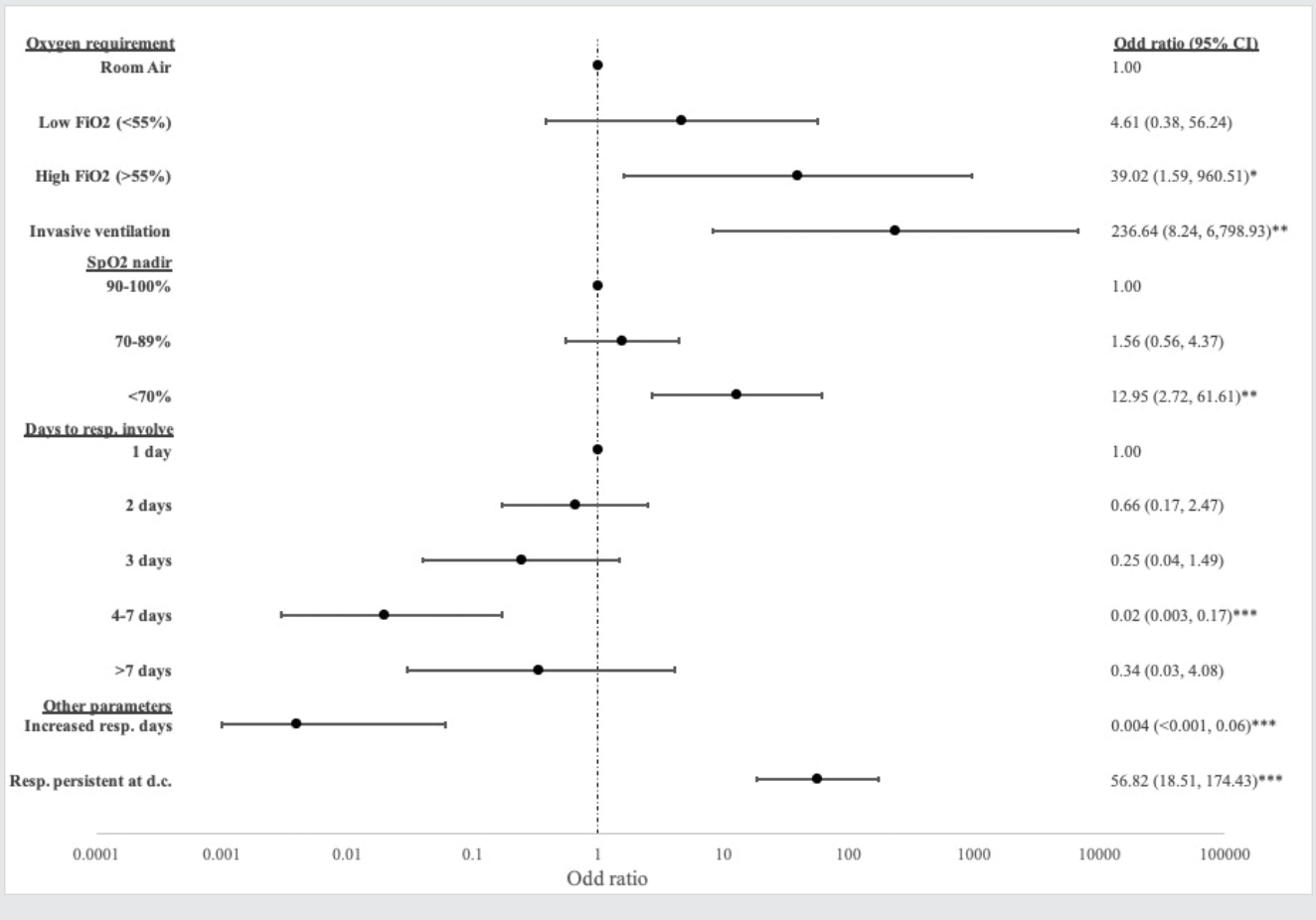
**TABLE 2**  
**Logistic regression analyses for mortality**

Variables	Model 1 Univariate OR (95% CI)	Model 2 Multivariate OR (95% CI)
<b>Demographics</b>		
Age (years)	1.05 (1.04, 1.07)***	1.07 (1.03, 1.11)**
Sex (female)	0.99 (0.72, 1.35)	—
Race/ethnicity		
Caucasian	1.00	1.00
African American	0.67 (0.44, 1.02)	0.82 (0.32, 2.13)
Hispanic	0.47 (0.32, 0.69)***	0.79 (0.30, 2.08)
East Asian	1.59 (0.68, 3.72)	0.22 (0.04, 1.36)
Southeast Asian	0.67 (0.22, 2.04)	0.17 (0.02, 1.63)
Other	1.53 (0.53, 4.40)	2.32 (0.18, 29.73)
Insurance		
Private	1.00	1.00
Uninsured/Emergency Medicaid	0.99 (0.59, 1.66)	1.17 (0.36, 3.76)
Regular Medicaid	1.78 (1.15, 2.77)*	1.87 (0.67, 5.22)
Medicare	3.48 (2.14, 5.66)***	2.23 (0.65, 7.71)
<b>Comorbidities</b>		
Tobacco		
Never	1.00	1.00
Former	1.47 (0.87, 2.48)	0.51 (0.15, 1.80)
Current	0.11 (0.02, 0.85)*	0.01 (0.001, 0.21)**
Unknown	2.45 (1.72, 3.51)***	1.20 (0.49, 2.95)
Vaping		
Never	1.00	1.00
Current	—	—
Unknown	1.10 (1.10, 1.50)**	1.15 (0.77, 1.72)
Obese (yes)	0.92 (0.67, 1.27)	—
CCI	1.35 (1.26, 1.44)***	1.07 (0.87, 1.33)
<b>Disease severity</b>		
qSOFA	1.73 (1.35, 2.22)**	1.04 (0.58, 1.88)
ICU (yes)	22.03 (13.67, 35.49)***	0.86 (0.11, 7.00)
Intubation admission (yes)	12.02 (5.27, 27.39)***	0.24 (0.05, 1.09)
Oxygen requirement hospitalization		
None	1.00	1.00
Low FiO <sub>2</sub> (≤ 55%)	5.42 (0.71, 41.38)	4.61 (0.38, 56.24)
High FiO <sub>2</sub> (> 55%)	49.47 (6.74, 363.05)***	39.02 (1.59, 960.51)*
Invasive mechanical ventilation	446.76 (59.79, 3338.44)***	236.64 (8.24, 6798.93)**
<b>Treatment management</b>		
Vasopressor (yes)	20.58 (11.93, 35.50)***	4.14 (1.34, 12.75)*
Antibiotic (yes)	1.86 (0.79, 4.37)	—
NSAID (yes)	1.35 (0.94, 1.93)	—
ACEi/ARBs (yes)	0.70 (0.42, 1.16)	—
Antiviral (yes)	4.47 (1.54, 13.02)**	1.87 (0.14, 25.05)
Antimalarial (yes)	0.83 (0.55, 1.25)	—
Steroid (yes)	1.87 (1.36, 2.57)***	0.92 (0.39, 2.15)
Convalescent plasma (yes)	1.56 (0.88, 2.74)	—
Interleukin inhibitor (yes)	1.83 (1.16, 2.90)*	0.51 (0.18, 1.45)
Anticoagulant (yes)	1.19 (0.82, 1.73)	—
<b>Organ involvement</b>		
Respiratory plus other organ systems	2.70 (2.35, 3.12)***	1.60 (1.20, 2.14)**
<b>Respiratory involvement</b>		
Oxygen saturation admission	—	
90–100		1.00
70–89		0.92 (0.39, 2.14)
<70		0.37 (0.05, 2.66)
Oxygen saturation nadir	—	
90–100		1.00
70–89		1.56 (0.56, 4.37)
<70		12.95 (2.72, 61.61)**
Respiratory proportion days involved	—	0.004 (<0.001, 0.06)***
Days to respiratory involvement	—	
1		1.00
2		0.66 (0.17, 2.47)
3		0.25 (0.04, 1.49)
4–7		0.02 (0.003, 0.17)***
>7		0.34 (0.03, 4.08)
Respiratory persistent involvement at discharge (yes)	—	56.82 (18.51, 174.43)***

Note: OR = odds ratio, CI = confidence interval, CCI = Charlson Comorbidity Index, qSOFA = quick sepsis related organ failure assessment, ICU = intensive care unit, FiO<sub>2</sub> = fraction of inspired oxygen, NSAID = nonsteroidal anti-inflammatory drug, ACEi = angiotensin-converting-enzyme inhibitors, ARB = angiotensin II receptor blockers, \*P < 0.05, \*\*P < 0.01, \*\*\*P < 0.001, Model 2 Nagelkerke R<sup>2</sup> = 0.85. Respiratory plus other organ systems is the number of organ systems involved.

FIGURE 1

Association of respiratory parameters with in-hospital mortality. Respiratory parameters include oxygen requirement in hospital, oxygen saturation (SpO<sub>2</sub>) nadir in hospital, days to respiratory (resp.) involvement, increased respiratory involvement days, and persistent respiratory involvement at discharge (d.c.). Odd ratios with error bars representing 95% confidence interval are expressed in logarithmic scale. All variables were adjusted to number of organ system involvement, age, sex, race/ethnicity, insurance status, comorbidities including smoking and vaping histories, obesity, Charlson Comorbidity Index, disease severity including quick sepsis related organ failure assessment, intensive care unit admission, intubation on admission, treatment management, and oxygen saturation on admission. Superscripts: the *P*-value levels are expressed in asterisks for \**P* < 0.05, \*\**P* < 0.01, and \*\*\**P* < 0.001. Abbreviations: resp. = respiratory; d.c. = discharge.



mortality and LOS in COVID-19 [1, 2, 5, 6, 15–17]. No studies have demonstrated this association after adjusting for all the involvement of other organ systems in COVID-19. We suggest that SARS-COV 2 is primarily a respiratory virus that affects the respiratory system; therefore, hospitalized COVID-19 patients who presented with severe respiratory symptoms were associated with worse prognosis.

We found that oxygen saturation nadir of <70% was associated with increased odds for mortality, whereas oxygen saturation nadir of 70%–89% during hospital stay was significantly associated with increased LOS. COVID-19 patients with oxygen saturation nadir of <70% have more critical disease, and their increased mortality is in line with other studies showing higher mortality in critically ill COVID-19 patients [1, 2]. In contrast, those with oxygen saturation nadir of 70%–89% during hospitalization had a noncritical but severe disease process and required longer hospital stay until recovery and discharge. This is consistent with studies showing that severe COVID-19 increases the LOS [16, 17]. We suggest that the oxygen saturation nadir may be used as a prognostic tool in hospitalized COVID-19 patients.

We found that an increased proportion of days of respiratory system involvement was associated with decreased odds of mortality and an increased LOS. Other studies have also shown that COVID-19 survivors, as compared to COVID-19 patients who died in the hospital, have prolonged hospital stays likely due to respiratory sequela [18, 19]. Our findings are similar to this pattern. We suggest that for many patients, respiratory involvement is appropriately managed during their hospital stay with improving patient survival and extended patient LOS.

We found that respiratory involvement on days 2, 3, 4–7, and >7 was associated with increased LOS compared with respiratory involvement found on day of admission, and respiratory involvement on days 4–7 was associated with decreased odds of mortality. The onset of dyspnea on days 4–7 is a typical presentation for COVID-19 patients [4, 8, 9]. Patients presenting with respiratory involvement on the first day of hospitalization likely presented during a later course of their illness. We suggest that our patients who developed respiratory involvement in the hospital presented to the hospital earlier in their course of illness. Admission to the hospital at the early course of their illness resulted in

**TABLE 3**  
**Linear regression analyses for length of stay**

Variables	Model 1 Univariate B (SE)	Model 2 Multivariate B (SE)
<b>Demographics</b>		
Age (years)	-0.001 (0.001)	—
Sex (female)	-0.08 (0.03)**	-0.04 (0.02)
Race/ethnicity		
Caucasian	Reference	Reference
African American	-0.04 (0.04)	-0.01 (0.03)
Hispanic	0.02 (0.03)	-0.002 (0.02)
East Asian	-0.16 (0.08)*	-0.08 (0.05)
Southeast Asian	0.02 (0.09)	0.05 (0.07)
Other	0.09 (0.09)	0.01 (0.07)
Insurance		—
Private	Reference	
Uninsured/Emergency Medicaid	0.02 (0.04)	
Regular Medicaid	-0.06 (0.04)	
Medicare	0.02 (0.04)	
<b>Comorbidities</b>		
Tobacco use		—
Never	Reference	
Former	0.01 (0.05)	
Current	0.07 (0.08)	
Unknown	0.03 (0.03)	
Vaping		—
Never	Reference	
Current	—	
Unknown	0.01 (0.01)	
Obese (yes)	-0.03 (0.03)	—
CCI	-0.004 (0.01)	—
<b>Disease severity</b>		
qSOFA	-0.01 (0.02)	—
ICU (yes)	0.24 (0.02)***	0.14 (0.05)**
Intubation admission (yes)	-0.03 (0.06)	—
Oxygen requirement hospitalization		
None	Reference	Reference
Low FiO <sub>2</sub> (≤ 55%)	0.11 (0.05)*	0.04 (0.03)
High FiO <sub>2</sub> (> 55%)	0.25 (0.04)***	-0.09 (0.06)
Invasive mechanical ventilation	0.35 (0.04)***	-0.08 (0.06)
<b>Treatment management</b>		
Vasopressor (yes)	0.21 (0.03)***	-0.004 (0.03)
Antibiotic (yes)	0.21 (0.06)**	0.13 (0.05)**
NSAID (yes)	0.10 (0.03)**	0.05 (0.02)*
ACEi/ARBS (yes)	0.01 (0.04)	—
Antiviral (yes)	0.22 (0.09)*	0.12 (0.06)
Antimalarial (yes)	0.10 (0.04)**	0.02 (0.03)
Steroid (yes)	0.33 (0.03)***	0.10 (0.02)***
Convalescent plasma (yes)	0.54 (0.05)***	0.21 (0.04)***
Interleukin inhibitor (yes)	0.42 (0.04)***	0.09 (0.04)*
Anticoagulant (yes)	0.30 (0.03)***	0.07 (0.03)*
<b>Organ involvement</b>		
Respiratory plus other organ systems	0.06 (0.01)***	0.02 (0.01)**
<b>Respiratory involvement</b>		
Oxygen saturation admission	—	
90–100		Reference
70–89		0.002 (0.03)
<70		-0.03 (0.06)
Oxygen saturation nadir	—	
90–100		Reference
70–89		0.07 (0.03)*
<70		0.05 (0.04)
Respiratory proportion days involved	—	0.90 (0.07)***
Days to respiratory involvement	—	
1		Reference
2		0.20 (0.03)***
3		0.33 (0.05)***
4–7		0.49 (0.05)***
>7		0.81 (0.07)***
Respiratory persistent involvement at discharge (yes)	—	-0.15 (0.02)***
Constant	—	-0.17 (0.07)*

Note: B = unstandardized beta, SE = standard error, CCI = Charlson Comorbidity Index, qSOFA = quick sepsis related organ failure assessment, ICU = intensive care unit, FiO<sub>2</sub> = fraction of inspired oxygen, NSAID = nonsteroidal anti-inflammatory drug, ACEi = angiotensin-converting-enzyme inhibitors, ARB = angiotensin II receptor blockers, \*P < 0.05, \*\*P < 0.01, \*\*\*P < 0.001, Model 2 adjusted R Square = 0.52. Respiratory plus other organ systems is the number of organ systems involved.

longer LOS until completion of disease course and treatment and allowed for sufficient early treatment and closer monitoring of their disease course, and thus lower mortality on days 4–7. Patients who developed respiratory symptoms >7 days were not associated with mortality. It is important to note that the small sample size of the >7 days group limits the interpretation of our findings.

We found that persistent respiratory involvement at discharge was associated with increased odds of mortality and decreased LOS. This occurred because almost all patients who died in the hospital had respiratory involvement at discharge, whereas COVID-19 survivors were more likely to have improved and some resolved respiratory dysfunction. As other studies showed that COVID-19 patients who died in the hospital tended to have shorter LOS than COVID-19 survivors [19], this supports our explanation for the decreased LOS in our patients.

Among COVID-19 patients with respiratory involvement, we found that increased age was significantly associated with increased odds for mortality, which is consistent with prior studies [2, 5, 20]. Our data showed that sex, race/ethnicity, and insurance status were not associated with mortality or LOS. Findings on the association of sex, race/ethnicity, and insurance status with mortality and LOS are mixed. Some studies found that male gender, and African-American and Hispanic race/ethnicity were associated with worse outcomes and increased mortality [2, 21], whereas other studies that adjusted for comorbidities and socioeconomic status did not find these negative associations [22–24]. Our adjusted analyses are consistent with the latter studies.

Surprisingly, we found that current tobacco use was associated with decreased odds of mortality. The results of the studies looking at the association between tobacco use and COVID-19 mortality are contradictory and inconclusive. Some studies reported that active smoking is associated with higher COVID-19 mortality [25, 26], others reported that current smoking is not associated with COVID-19 mortality [27], and some reported decreased COVID-19 mortality and severity in active smokers [5, 28]. The discrepancy of association in multiple other studies is due to limitations of studies on smoking and COVID-19 severities. Most studies did not separate current and former smokers, and the reported prevalence in these studies was lower than the country's smoking prevalence [26]. Although our data suggest that active smoking may be protective for COVID-19 mortality, it should be interpreted with caution as close to one-quarter of our patients had unknown tobacco use status. Definitive risk versus protection of tobacco use in COVID-19 should be further investigated.

We found that ICU level of care was not associated with mortality, but was significantly associated with increased LOS. Multiple studies with COVID-19 patients reported that ICU admission increases mortality [4, 17]. In our study, the ICU level of care was provided to patients requiring close monitoring of their respiratory status in addition to patients with critical illness. This might have resulted in ICU level of care not having an impact on mortality in this patient group; however, we found an increased LOS in these patients. Our study is consistent with others that show ICU stay in COVID-19 is associated with increased LOS [29], likely because patients have a longer of stay in the ICU.

We found that  $\text{FiO}_2 >55\%$  and mechanical ventilation were each associated with increased odds for mortality. These findings are consistent with other studies [2, 5]. We found no association between CCI and qSOFA adjusted for other variables and mortality. CCI was designed to estimate mortality based on chronic illnesses but not tailored to estimate risk in COVID-19 [11]. Multiple disease severity scoring systems were examined to assess COVID-19 prognosis, but none was validated or adopted for common use [30]. Our finding of no association between clinical scoring systems such as CCI and qSOFA and COVID-19 mortality is consistent with other studies [30, 31].

We found that vasopressor use was significantly associated with increased odds for mortality. The increased mortality with vasopressor use in COVID-19 is consistent with other studies [32]. We found that the use of antibiotics, NSAIDs, steroids, convalescent plasma, IL6 inhibitors, and anticoagulants was associated with increased LOS but not with mortality. Other studies showed no difference in hospital LOS with steroid, convalescent plasma, or IL6 inhibitor use [33–35]. We attribute the

association with increased LOS in our study to the need of staying in the hospital to complete the treatment course, which is supported by other studies [16, 36]. We did not find any association between antiviral use and mortality likely due to the small sample size and because remdesivir was not available at the early phase of the pandemic. Unlike other studies [37], we did not find any mortality benefit of steroid use as there were no standardized guidelines for steroid administration during the early phase of the pandemic. Inconsistent and varying administration of steroids might not have provided protection against COVID-19.

### Study limitations

Our study had several limitations. First, this was a retrospective study conducted at a single center. We studied a large and diverse population in the New York metropolitan area. However, a multi-center study could provide a larger sample and be more representative of the general population in the United States. Further prospective studies should also be conducted to investigate the causal relationships of respiratory parameters. Second, objective laboratory values such as arterial blood gas findings were not available, as these laboratory tests were not routinely obtained during the pandemic. Future studies should investigate respiratory laboratory tests in COVID-19 patients and their association with clinical outcomes. Third, as the study was conducted in the early phases of the pandemic, there is no set standardized treatment procedure, therefore making it difficult to assess the effect of treatment.

### CONCLUSION

We found that respiratory involvement adjusted for all other organ system involvement was significantly associated with increased odds of mortality and increased LOS. COVID-19 patients with respiratory involvement had increased mortality with  $\text{FiO}_2 >55\%$  and mechanical ventilation during hospitalization. Oxygen saturation nadir of 70%–89% during hospital stay was significantly associated with increased LOS, whereas oxygen saturation nadir of <70% was associated with increased odds for mortality. An increased proportion of days in hospital of respiratory system involvement was associated with decreased odds for mortality and increased LOS. Respiratory involvement on days 4–7 was associated with decreased odds for mortality, and respiratory involvement on day >1 was associated with increased LOS compared to respiratory involvement found on day of admission. Persistent respiratory involvement at discharge was associated with increased odds for mortality and decreased LOS. These data may provide insight into assessing clinical prognosis of tailoring treatment for COVID-19 hospitalized patients with respiratory involvement.

### DISCLOSURES

#### Contributors

EL: study design, data acquisition, data interpretation, drafting manuscript, manuscript approval  
SGP: study design, data acquisition, data interpretation, revising manuscript, manuscript approval  
DGH: data acquisition, revising manuscript, manuscript approval  
YNP: data acquisition, revising manuscript, manuscript approval  
JF: study design, data interpretation, data analysis, revising manuscript, manuscript approval  
SR: study design, data interpretation, revising manuscript, manuscript approval

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#### Competing interests

All authors have completed the ICMJE uniform disclosure form at [www.icmje.org/coi\\_disclosure.pdf](http://www.icmje.org/coi_disclosure.pdf) and declare: no financial relationships with any organizations that might have an interest in the submitted work in the previous 3 years; no other relationships or activities that could appear to have influenced the submitted work.

### Ethical approval

The IRB of the local institution approved the study. A waiver for informed consent was received due to the retrospective nature of the study.

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