RESEARCH ARTICLE

Risk factors for mortality in COVID-19 patients in a community teaching hospital

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Abstract

As of December 2020, there were over 450,000 confirmed coronavirus disease 2019 (COVID-19) cases in New York City (NYC) with approximately 25,000 deaths. Previous literature identified advanced age, higher severity of illness, elevated inflammatory biomarkers, acute organ dysfunction, comorbidities, and presentation from long-term care facility as risk factors for mortality in patients from Wuhan, China, and the United States. Additional studies conducted in NYC are warranted to confirm these findings. The objective of this study was to assess the risk factors for in-hospital mortality in patients with confirmed COVID-19 infections. This was a retrospective case-control study at The Brooklyn Hospital Center, a 464-bed community teaching hospital. Adult patients with a confirmed COVID-19 infection and who received at least 24 h of COVID-19 therapy were included. Univariate and multivariate logistic regression analyses were conducted to identify the risk factors for in-hospital mortality. Two-hundred and eighty four patients were included, of whom 95 (33.5%) were non-survivors and 189 (66.5%) patients were survivors. Multivariate analysis showed higher in-hospital mortality with advanced age (odds ratio [OR] 6.476; 95% confidence interval [CI], 1.827–22.953), presentation from long-term care facility (OR 4.259; 95% CI 1.481–12.250), elevated total bilirubin (OR 4.947; 95% CI 1.048–23.350), vasopressor initiation (OR 36.262; 95% CI 5.319–247.216), and development of renal failure (OR 36.261; 95% CI 2.667–493.046). Risk factors associated with mortality for patients with COVID-19 in a community teaching hospital included advanced age, vasopressor initiation, development of renal failure, elevated total bilirubin, and presentation from long-term care facility.

KEYWORDS
COVID-19, mortality, outcomes, risk factors

1 | INTRODUCTION

Coronavirus disease 2019 (COVID-19) is caused by a novel enveloped RNA beta-coronavirus named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). COVID-19 is primarily spread through respiratory droplets from direct person-to-person transmission, and was first identified in Wuhan, China.[1] COVID-19 subsequently spread to other areas of the world, including Europe and the United States.[2] New York City (NYC) was one of the first regions in the United States to experience

major outbreaks of COVID-19 infections due to its dense population and urbanized environment. As of December 2020, there were over 450,000 confirmed COVID-19 cases in NYC with approximately 70,000 hospitalizations and 25,000 deaths.[3] The crude fatality rate was 9.2% among all confirmed cases and 32.1% among hospitalized patients in NYC within the first three months of the COVID-19 pandemic. Hospital admissions peaked during the week of March 29th and then decreased steadily towards the end of April.[4]

Zhou et al.[5] first assessed patients with COVID-19 infections in several hospitals in Wuhan, China and found older age, high Sequential Organ Failure Assessment score, and D-dimer more than 1 µg/ml as independent risk factors for in-hospital mortality. Subsequently, Albitar et al conducted a cross sectional study using worldwide open access data in which they found that male sex, advanced age, comorbidities (e.g., hypertension and diabetes mellitus), and patients located in America were independent risk factors for mortality.[6] Two multicentered studies in NYC and Long Island, NY evaluated the clinical characteristics and outcomes of patients with COVID-19 infections early on during the outbreak in NYC, but neither study assessed risk factors for mortality.[7,8] In addition, a prospective multicenter observational study conducted in NYC found advanced age, chronic cardiac disease, chronic pulmonary disease, increased interleukin-6, and D-dimer as independent risk factors of in-hospital mortality.[9] Recently, a multicenter retrospective study including over 500 hospitals conducted throughout the United States found that older age was most strongly associated with death. Likewise, male sex, patients transferred from long-term care facilities, and patients from hospitals from the northeastern portion of the United States were associated with in-hospital mortality in this retrospective study.[10] Although these findings help determine patients at risk for mortality among the United States and NYC population, subsequent studies are needed to confirm these findings.

In this retrospective case-control single-center analysis, we assessed clinical characteristics, outcomes and risk factors for mortality in hospitalized patients with confirmed COVID-19 infections in NYC.

2 | METHODS

2.1 | Study design and participants

This retrospective study took place at The Brooklyn Hospital Center (TBHC), a 464-bed community teaching hospital. Adult patients, 21 years of age or older, were included if they were admitted to TBHC between March 1, 2020 to April 15, 2020 with moderate to severe COVID-19 infection confirmed by reverse transcriptase-polymerase chain reaction (RT-PCR) and received at least 24 h of COVID-19 therapy. The study period was chosen to evaluate patients outcomes at the peak of the pandemic and due to the significant decrease in patients hospitalized for COVID-19 at our institution following this period. Moderate to severe COVID-19 infection was defined as fulfilling at least

one of the following criteria: radiographic evidence of pneumonia as per radiologist's final report, oxygen saturation less than 94% on room air, or requiring supplemental oxygen. Patients were excluded if death occurred before COVID-19 RT-PCR test result or if they were still admitted at the time of data analysis.

2.2 | Study oversight

This study was approved by The Brooklyn Hospital Center Institutional Review Board (IRBNet ID: 1609888-1). Informed consent was waived for retrospective review of patient charts.

2.3 | Study outcomes and definitions

The primary endpoint was risk factors for mortality in patients with COVID-19. The secondary endpoints were hospital and ICU length of stay and mortality, disease severity at Day 7 from primary antiviral therapy initiation, 30-day readmission, development of renal failure, initiation of renal replacement therapy, development of prolonged QTc, ventricular fibrillation, and ventricular tachycardia.

COVID-19 diagnosis date was defined as the date of COVID-19 primary antiviral therapy order entry into the electronic medical record. Primary COVID-19 therapy was defined as the first pharmacologic agent administered to the patient for the treatment of COVID-19 infection. Disease severity was defined by the seven-category ordinal scale consisting of the following categories: 1, not hospitalized with resumption of normal activities; 2, not hospitalized, but unable to resume normal activities; 3, hospitalized, not requiring supplemental oxygen; 4, hospitalized, requiring supplemental oxygen; 5, hospitalized, requiring nasal high-flow oxygen therapy, noninvasive mechanical ventilation, or both; 6, hospitalized, requiring ECMO, invasive mechanical ventilation, or both; or 7, death.[11] Renal failure was defined as acute kidney injury (AKI) Stage 3, which is an increase in serum creatinine greater than or equal to three times from baseline, or an increase greater than or equal to 0.5 mg/dL if the baseline serum creatinine was greater than 4 mg/dL.[12] Development of prolonged QTc was defined as increase of baseline QTc by greater than or equal to 60 ms or increase of baseline QTc greater than 500 ms (if baseline was less than 500 ms).[13] Additional definitions can be found in the Supplementary Material.

2.4 | Laboratory testing

Laboratory testing for COVID-19 infection was done using the Abbott RealTime SARS-CoV-2 assay, a RT-PCR test, of nasopharyngeal or oropharyngeal swab samples. Testing was performed at the New York State Department of Health from March 1st to March 28th, 2020 and at TBHC from March 29th, 2020 to the end of the study period.

2.5 | Data collection

Data collection and study outcomes were evaluated until May 28, 2020, which is 43 days from the date of the last patient admission. Baseline demographic data, laboratory measurements, imaging studies, concomitant infection (e.g., bacterial and/or influenza), hospitalization information (e.g., location before admission, hospitalization dates, hospital location, etc.), type of consultation (infectious diseases and/or pulmonary critical care), disease severity at baseline, treatment (e.g., primary antiviral therapy, adjunctive therapy, antibiotic therapy, influenza therapy, new-start therapeutic anticoagulation, e.g., heparin, enoxaparin, direct oral anticoagulant [DOAC], or warfarin), vasopressors, and glucocorticoids) and outcomes were collected from the electronic medical record, Allscripts®, and stored on an encrypted Microsoft Excel® file.

2.6 | Statistical analysis

Two-tailed t-tests, Mann–Whitney U, χ^2, or Fisher's exact tests were performed to compare differences between survivors and non-survivors where appropriate; missing data were excluded from data summary and analysis. An α less than .05 was considered statistically significant for all tests. All analyses were conducted using SPSS (version 27.0.; IBM Corp.).

Univariate logistic regression was first used to determine the odds ratios (ORs) and 95% confidence intervals (CIs) for risk factors associated with in-hospital mortality. Nonredundant variables with a p value less than or equal to .20 on univariate logistic regression analysis were included in the multivariate logistic regression analysis. To avoid overfitting in the multivariate logistic regression model, seventeen independent variables were chosen based on number of deaths in our study.[14] The events per variable was between 5 and 9 thus leading to the inclusion of additional variables compared with previous literature in multivariate logistic regression analysis without exacerbating the risk of relative bias, type I error, and lower confidence interval coverage.[5,9,14]

2.6.1 | Variables included in multivariate logistic regression analysis

Eleven variables were selected based on previous literature that identified these variables as significant risk factors for mortality by multivariate logistic regression: advanced age[5,6,9,10]; presentation from long-term care facility[10]; elevated D-dimer[5,9]; chronic cardiac disease (i.e., coronary artery disease or congestive heart failure) and chronic obstructive pulmonary disease or interstitial disease[9,10]; elevated total bilirubin, aspartate aminotransferase (AST), and alanine aminotransferase (ALT)[15]; male sex[6,10,16]; hypertension[6,17,18]; AKI[10,19]; and diabetes.[6,10] Our study included baseline serum creatinine greater than or equal to 1.5 mg/dL and development of renal failure to assess whether baseline kidney dysfunction is associated with in-hospital mortality. In addition, initiation of renal replacement therapy (RRT) was included as patients in AKI that require RRT have a higher risk of death.[20] ICU admission, invasive mechanical ventilation, and vasopressor initiation were included as literature has shown higher frequency of these variables associated with non-survivors compared with survivors.[9]

2.6.2 | Variables excluded in multivariate logistic regression analysis

Specialist consultation, respiratory rate (RR) greater than or equal to 25 breaths per minute, systolic blood pressure (SBP) less than or equal to 90 mmHg, heart rate (HR) greater than or equal to 125 beats per minute, white blood cell count, lymphocyte count, platelet count, serum ferritin, C-reactive protein, troponin, QTc interval, and bacteremia were not included as prior studies have not shown these categories as independent risk factors for mortality and the investigators avoided risk of overfitting.[5,9,14] Similarly, primary antiviral therapy, missed two doses or more of primary antiviral therapy, new start therapeutic anticoagulation, adjunctive therapy, concomitant antibiotic therapy, and glucocorticoid initiation were excluded.

3 | RESULTS

Between March 1st and April 15th, 2020, 284 adults were admitted to The Brooklyn Hospital Center with laboratory-confirmed COVID-19 infections that met inclusion criteria, of which 95 (33.5%) were non-survivors and 189 (66.5%) were survivors.

The majority of demographics and baseline characteristics were different among non-survivors and survivors (Table 1). It should be noted that nonsurvivors were of older age ($p < .001$) and were more often males ($p = .040$), presenting from a nursing home ($p < .001$), had a specialist consultation ($p < .001$), and were admitted to the ICU ($p < .001$). Moreover, nonsurvivors also had a significantly higher rate of coronary artery disease, and diabetes compared with survivors ($p < .001$, $p = .003$, respectively). Furthermore, nonsurvivors had significantly worse baseline vital signs, such as, tachypnea (49, 51.6%), tachycardia (24, 25.3%), and hypotension (25, 26.3%) compared with survivors ($p < .001$ for all variables). In regard to baseline laboratory and inflammatory parameters, pertinent findings were that non-survivors had more lymphopenia ($p = .007$), D-dimer > 1 μg/ml ($p = .048$), CRP > 100 mg/L ($p = .039$), serum ferritin less than 300 μg/L ($p = .048$); refer to Table 1 for additional significant findings. Likewise, disease severity at baseline differed significantly, in that, 21 (22.1%) patients in the nonsurvivors group required invasive mechanical ventilation at baseline compared with two (1.0%) patients in the survivors group ($p < .001$). On the contrary, 44 (23.3%) patients in the survivor group did not require supplemental oxygen compared with 11 (11.6%) patients in the nonsurvivors group ($p = .025$).

TABLE 1 Demographics and baseline characteristics of patients with COVID-19[a]

	Total (n = 284)	Nonsurvivor (n = 95)	Survivor (n = 189)	p value
Patient characteristics				
Age, years, mean ± SD	67.0 ± 14.5	72.3 ± 11.6	64.3 ± 15.0	<.001
Male sex	155 (54.6)	60 (63.2)	95 (50.3)	.040
Actual body weight, kg	80.2 [67.5–97.0]	78.5 [65.6–90.8]	81.6 [68.0–98.0]	.158
BMI, kg/m^2	27.9 [24.2–34.0]	27.7 [24.2–32.6]	28.0 [24.2–34.1]	.282
BMI ≥ 30 kg/m^2	107 (37.8)	31 (33.0)	76 (59.8)	.244
Pregnant	2 (0.7)	0 (0.0)	2 (1.1)	.553
Race or ethnic group				
White	14 (4.9)	7 (7.4)	7 (3.7)	.244
Black	179 (63.0)	58 (61.0)	121 (64.0)	.696
Asian	9 (3.2)	5 (5.3)	4 (2.1)	.167
Hispanic	23 (8.1)	8 (8.4)	15 (7.9)	1.000
Other/declined	59 (20.8)	17 (17.9)	42 (22.3)	.441
Healthcare worker	3 (1.1)	1 (1.1)	2 (1.1)	1.000
Location before admission				
Home	217 (76.4)	61 (64.2)	156 (82.5)	.001
Nursing home	55 (19.4)	32 (33.6)	23 (12.2)	<.001
Assisted living facility	8 (2.8)	1 (1.1)	7 (3.7)	.275
Other	4 (1.4)	1 (1.1)	3 (1.6)	1.000
Specialist consultation	173 (60.9)	75 (78.9)	98 (51.9)	<.001
Infectious diseases	104 (36.6)	25 (26.3)	79 (41.8)	0.013
Pulmonary critical care	39 (13.7)	29 (30.5)	10 (5.3)	<.001
Both	30 (10.6)	21 (22.1)	9 (4.8)	<.001
ICU admission	62 (21.8)	48 (50.5)	14 (7.4)	<.001
Current smoker[b]	13 (5.7)	4 (6.6)	9 (5.4)	.750
Comorbidities[c]				
Hypertension	205 (73.0)	72 (78.3)	133 (70.4)	.164
Coronary artery disease	47 (16.7)	28 (30.4)	19 (10.1)	<.001
Chronic respiratory disease[d]	44 (15.7)	17 (18.5)	27 (14.3)	.365
Diabetes	123 (43.8)	52 (56.5)	71 (37.6)	.003
Cancer	10 (3.6)	2 (2.2)	8 (4.2)	.506
Immunocompromised[e]	10 (3.6)	6 (6.5)	4 (2.1)	.085
Fever (>38.0°C)	126 (44.4)	46 (48.4)	80 (42.3)	.376
RR > 24 breaths per minute	81 (28.5)	49 (51.6)	32 (16.9)	<.001
HR ≥ 125 beats per minute	38 (13.4)	24 (25.3)	14 (7.4)	<.001
SBP < 90 mmHg	32 (11.3)	25 (26.3)	7 (3.7)	<.001
White blood cell count (×10^9/L)[f]	7.7 [5.1 – 10.9]	9.0 [6.9 – 13.3]	7.2 [4.9 – 9.7]	<.001
<4	40 (14.1)	13 (13.7)	27 (14.3)	1.000
4–10	160 (56.3)	40 (42.1)	120 (63.5)	<.001
>10	84 (29.6)	42 (44.2)	42 (22.2)	<.001
Lymphocyte count (x10^9/L)[f]	0.8 [0.6 – 1.2]	0.7 [0.5 – 1.0]	0.9 [0.6 – 1.2]	.005
<1.0	175 (61.6)	69 (72.6)	106 (56.1)	.007
Platelets (k/cmm)[f]	201 [152 – 263]	182 [141 – 254]	215 [161 – 275]	.015
<150	69 (24.3)	27 (28.4)	42 (22.2)	.305
D-Dimer (mcg/mL)[f]	2.1 ± 1.5	3.3 ± 1.5	1.6 ± 1.3	<.001
>1	39 (66.1)	14 (87.5)	25 (58.1)	.048

	Total	Nonsurvivor	Survivor	p value
	(n = 284)	(n = 95)	(n = 189)	
Serum ferritin (mcg/L)[f]	804 [399 – 2292]	1139 [556 – 3089]	688 [341 -1813]	.001
>300	216 (80.9)	79 (87.8)	137 (77.4)	.048
CRP (mg/L)[f]	119 [68 – 198]	140 [84 – 248]	109 [61 -172]	.001
>100	163 (58.8)	63 (67.7)	100 (54.4)	.039
AST (units/L)[f]	49[35–77]	57[39–90]	44[32–71]	.006
>40	157 (60.6)	62 (71.3)	95 (55.2)	.013
ALT (units/L)[f]	28[19–47]	29[20–51]	26[18–46]	.210
>40	84 (32.4)	31 (35.6)	53 (30.8)	.483
Total bilirubin (mg/dL)[f]	0.6 [0.4 – 0.8]	0.6 [0.4 – 1.0]	0.6 [0.4 – 0.8]	.235
> 1.2	22 (8.5)	13 (14.9)	9 (5.2)	.011
Serum creatinine (mg/dL)[f]	1.2 [0.8 – 2.4]	1.7 [1.0 – 3.8]	1.1 [0.8 – 1.9]	<.001
>1.5	112 (39.4)	53 (55.8)	59 (31.2)	<.001
Troponin (ng/ml)[f]	0.03 [0.01 – 0.11]	0.07 [0.02 – 0.19]	0.02 [0.01 – 0.06]	<.001
>0.5	22 (8.1)	13 (14.1)	9 (5.0)	.017
QTc interval[g] (ms)	447 [428 – 470]	449 [430 – 479]	447 [427 – 467]	.269
<470	204 (75.3)	62 (67.4)	142 (79.3)	.037
470–500	41 (15.1)	20 (21.7)	21 (11.7)	.033
>500	26 (9.6)	10 (10.9)	16 (9.0)	.665
Disease severity at baseline[h]				
3	55 (19.4)	11 (11.6)	44 (23.3)	.025
4	183 (64.4)	50 (52.6)	133 (70.4)	.004
5	23 (8.1)	13 (13.7)	10 (5.3)	.020
6	23 (8.1)	21 (22.1)	2 (1.0)	<.001
Positive chest imaging	251 (88.3)	87 (91.6)	164 (86.8)	.326
Ground-glass opacity	102 (35.9)	37 (39.0)	65 (34.4)	.512
Bilateral or multifocal infiltrates/opacities	149 (52.4)	50 (52.6)	99 (52.4)	1.000
Concomitant Infections	257 (90.5)	90 (94.7)	167 (88.4)	.091
Bacterial	202 (71.1)	71 (74.7)	131 (69.3)	.405
Influenza	2 (0.7)	0 (0.0)	2 (1.1)	.553
Both	53(18.7)	19 (20.0)	34 (18.0)	.747
Bacteremia	9 (3.2)	9 (9.5)	0 (0.0)	<.001

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; CRP, C-reactive protein; HR, heart rate; ICU, intensive care unit; RR, respiratory rate; SBP, systolic blood pressure.

[a]Data is presented as n (%) and median [interquartile range] unless specified otherwise.

[b]55 patients (34 non-survivors and 21 survivors) were excluded due to unknown smoking history.

[c]Three nonsurvivors were excluded from analysis since they were incapacitated on admission.

[d]Chronic respiratory disease was defined as chronic obstructive pulmonary disease (COPD), asthma, or chronic interstitial lung disease.

[e]Immunocompromised was defined as HIV and CD4 count less than 200 cells/mm^3, receipt of chronic steroids defined as ≥10 mg prednisone equivalent daily, or other immunosuppressive therapies.

[f]Patients with unavailable laboratory parameters were excluded from analysis.

[g]Electrocardiograms were not performed in 13 patients (3 nonsurvivors and 10 survivors) and were excluded from analysis.

[h]Disease severity was defined by the seven-category ordinal scale consisting of the following categories: 3, hospitalized, not requiring supplemental oxygen; 4, hospitalized, requiring supplemental oxygen; 5, hospitalized, requiring nasal high-flow oxygen therapy, noninvasive mechanical ventilation, or both; 6, hospitalized, requiring ECMO, invasive mechanical ventilation, or both).

Primary antiviral therapies were comparable amongst non-survivors and survivors, with the exception of the use of lopinavir/ritonavir, whereas duration of therapies were similar for both groups (Table 2). The most common primary antiviral combination was hydroxychloroquine (HCQ) and azithromycin. Nonsurvivors had a higher frequency of two or more missed doses of the primary anti-viral regimen with 23 (24.2%) patients compared with 11 (5.8%) patients among survivors, respectively. Antibiotics were frequently

TABLE 2 Treatment[a]

	Total	Nonsurvivor	Survivor	p value
	(n = 284)	(n = 95)	(n = 189)	
Primary antiviral therapy				
Hydroxychloroquine (HCQ)	44 (15.5)	15 (15.8)	29 (15.3)	1.000
HCQ and azithromycin	234 (82.4)	76 (80.0)	158 (83.6)	.510
Lopinavir-ritonavir	3 (1.0)	3 (3.1)	0 (0.0)	.037
Multiple therapies[b]	3 (1.0)	1 (1.1)	2 (1.1)	1.000
Time to initiation of antiviral therapy, h	4.98 [2.27–8.72]	5.60 [2.50–10.74]	4.75 [2.92–7.02]	.199
Duration of therapy (days), mean ± SD	5.28 ± 2.83	5.19 ± 2.63	5.33 ± 2.93	.697
Missed 2 or more doses	34 (12.0)	23 (24.2)	11 (5.8)	<.001
Medication route issue	7 (2.5)	6 (6.3)	1 (0.5)	.006
Intolerance	0 (0.0)	0 (0.0)	0 (0.0)	1.000
Adverse event	0 (0.0)	0 (0.0)	0 (0.0)	1.000
Not documented	27 (9.5)	17 (17.9)	10 (5.3)	.001
Adjunctive therapy				
Tocilizumab	20 (7.0)	13 (13.7)	7 (3.7)	.003
IVIG	4 (1.4)	4 (4.2)	0 (0.0)	.012
Convalescent plasma	5 (1.8)	3 (3.2)	2 (1.1)	.338
Concomitant antibiotic therapy	257 (90.5)	90 (94.7)	167 (88.4)	.091
MDRO coverage	115 (40.5)	56 (58.9)	59 (31.2)	<.001
New-start therapeutic anticoagulation	54 (19.0)	29 (30.5)	25 (13.2)	<.001
Enoxaparin	19 (6.7)	7 (7.4)	12 (6.3)	.803
Heparin	31 (10.9)	21 (22.1)	10 (5.3)	<.001
Warfarin	0 (0.0)	0 (0.0)	0 (0.0)	1.000
DOAC	4 (1.4)	1 (1.0)	3 (1.6)	1.000
Glucocorticoids initiation	97 (34.2)	44 (46.3)	53 (28.0)	.003
Vasopressors initiation	63 (22.2)	52 (54.7)	11 (5.8)	<.001
Multiple therapies[b]	42 (14.7)	39 (41.0)	3 (1.6)	<.001

Abbreviations: DOAC, direct oral anticoagulant; IVIG, intravenous immunoglobulin; MDRO, initiation of antibiotics for the treatment of infections caused by methicillin-resistant *Staphylococcus aureus* (MRSA) or *Pseudomonas aeruginosa*.

[a]Data is presented as n (%) and median [interquartile range] unless specified otherwise.

[b]Multiple therapies defined as two or more pharmacological agents.

administered to all patients, however, nonsurvivors received significantly more broad-spectrum antibiotics with MRSA or *Pseudomonas aeruginosa* activity. In addition, glucocorticoids, vasopressors, initiation of any therapeutic anticoagulation, and heparin initiation differed significantly between nonsurvivors and survivors.

We included available data from all patients (95 nonsurvivors and 189 survivors) in univariate and multivariate logistic regression analyses (Table 3). D-dimer was not included in the multivariate logistic regression analysis even though it was statistically significant through univariate logistic regression analysis as this parameter had only 59 patients whom had the variable obtained, which would limit the representation of the patient population for a predicator of mortality. ALT was not statistically significant on univariate logistic regression analysis (p = .483) as compared with other pertinent liver

injury markers (e.g., total bilirubin and AST) and therefore was excluded from multivariate logistic regression analysis. Our study included 15 variables in multivariate logistic regression analysis after the exclusion of D-dimer and ALT. Multivariate logistic regression identified advanced age (OR 6.476; 95% CI 1.827–22.953), presentation from long-term care facility (OR 4.259; 95% CI 1.481–12.250), elevated total bilirubin (OR 4.947; 95% CI 1.048–23.350), vasopressor initiation (OR 36.262; 95% CI 5.319–247.216), and development of renal failure (OR 36.261; 95% CI 2.667–493.046) as independent risk factors for mortality.

The average ICU length of stay amongst survivors and nonsurvivors was 10.71 ± 7.58 days and 8.85 ± 5.65 days, respectively (p = .321) (Table 4). The median hospital length of stay for survivors was 7 days (IQR 4.0–13.0 days) with 23 (12.8%) survivors being

Characteristics	Univariate logistic regression Odds ratio (95% CI)	p value	Multivariate logistic regression Odds ratio (95% CI)	p value
Long-term care facility[a] before admission	2.821 (1.587–5.013)	<.001	4.259 (1.481–12.250)	.007
ICU admission	12.766 (6.488–25.119)	<.001	–	–
Invasive mechanical ventilation	26.534 (6.069–115.999)	<.001	–	–
Age > 65 years	3.111 (1.824–5.308)	<.001	6.476 (1.827–22.953)	.004
Male	1.696 (1.024–2.811)	.040	–	–
Hypertension	1.516 (0.844–2.722)	.164	–	–
Coronary artery disease	3.914 (2.044–7.495)	<.001	–	–
Chronic respiratory disease[b]	1.360 (0.699–2.646)	.365	–	–
Diabetes	2.161(1.302–3.585)	.003	–	–
AST (units/L) > 40	2.010 (1.156–3.495)	.013	–	–
Total bilirubin (mg/dL) > 1.2	3.182 (1.302–7.773)	.011	4.947 (1.048–23.350)	.043
Serum creatinine (mg/dL) > 1.5	2.780 (1.672–4.623)	<.001	–	–
Vasopressor initiation	19.569 (9.423–40.638)	<.001	36.262 (5.319–247.216)	<.001
Development of renal failure	31.923 (9.359–108.890)	<.001	36.261 (2.667–493.046)	.007
Initiation of renal replacement therapy	8.505 (2.304–31.399)	.001	–	–

Abbreviations: AST, aspartate aminotransferase; ICU, intensive care unit.

[a]Long-term care facility was defined as nursing home or assisted living facility

[b]Chronic respiratory disease was defined as chronic obstructive pulmonary disease (COPD), asthma, or chronic interstitial lung disease.

readmitted within 30 days for the same initial complaint. By Day 7, there was a significantly higher frequency of survivors who were not hospitalized, and not requiring supplemental oxygen compared with non-survivors ($p < .001$, $p = .015$, respectively). However, non-survivors had a significantly higher association of invasive mechanical ventilation and death compared to survivors by Day 7 ($p < .001$, $p < .001$, respectively). Development of renal failure, initiation of new start renal replacement therapy, and incidence of ventricular fibrillation or ventricular tachycardia were significantly higher in non-survivors compared to survivors. Lastly, cardiac adverse events such as, increase in QTc by greater than 60ms and greater than 500 ms were comparable between the groups.

As there is limited literature that identified patients transferred from a long-term care facility as an independent risk factor for mortality in patients with COVID-19,[10] a post hoc analysis was conducted to further explore this finding (see Table S1). Variables that were included in the exploratory analysis were patient characteristics (e.g., age, sex, and comorbidities). Long-term care facility patients were significantly older compared to non-long-term care

facility patients, 75.0 ± 10.1 versus 64.8 ± 14.8 years old ($p < .001$), respectively. In terms of comorbidities, patients presenting from long-term care facility had a higher prevalence of hypertension, coronary artery disease, and chronic respiratory disease ($p < .035$, $p < .001$, and $p < .029$, respectively). However, sex, diabetes, cancer, and immunocompromising disease states were found to be comparable amongst long-term care facility patients and non-long-term care facility patients.

4 | DISCUSSION

Our retrospective case-control study represents one of the largest cohorts of patients with COVID-19 infections specifically in NYC assessing risk factors for in-hospital mortality through multivariate logistic regression. We demonstrated advanced age, AKI, elevated total bilirubin, and presentation from long-term care facility as risk factors for in-hospital mortality through multivariate logistic regression analysis, which are similar to the findings of previous

TABLE 4 Outcomes[a]

	Total (n = 284)	Nonsurvivor (n = 95)	Survivor (n = 189)	p value
Hospital length of stay, days	–	–	7.0 [4.0–13.0]	–
ICU length of stay, days, mean ± SD	9.27 ± 6.12	8.85 ± 5.65	10.71 ± 7.58	.321
Disease severity characteristics (Day 7)[b]				
2	101 (35.6)	0 (0.0)	101 (53.4)	<.001
3	21 (7.4)	2 (2.1)	19 (10.1)	.015
4	60 (21.1)	14 (14.7)	46 (24.3)	.066
5	22 (7.7)	5 (5.3)	17 (9.0)	.349
6	30 (10.6)	24 (25.3)	6 (3.2)	<.001
7	50 (17.6)	50 (52.6)	0 (0.0)	<.001
Hospital mortality (%)	95 (33.5)	95 (100.0)	–	–
Time to mortality, days	–	7.34 [4.87–11.39]	–	–
ICU mortality (%)	–	39 (41.1)	–	–
COVID-19-related mortality (%)	–	95 (100.0)	–	–
Discharged (%)	189 (66.5)	–	189 (100.0)	–
30-day readmission (%)[c]	23 (8.1)	–	23 (12.8)	–
Increase in QTc by >60 ms[d]	14 (9.0)	7 (10.1)	7 (8.1)	.779
Increase in QTc to > 500 ms (if baseline is <500 ms)[d]	12 (7.7)	5 (7.2)	7 (8.1)	1.000
Ventricular fibrillation or ventricular tachycardia (%)	4 (1.4)	4 (4.2)	0 (0.0)	.012
Development of renal failure[e]	33 (13.2)	30 (36.6)	3 (1.8)	<.001
Time to renal failure, days	3.83 [1.87–5.20]	3.88 [1.88–7.02]	1.94 [1.64–2.29]	.188
Initiation of renal replacement therapy[f]	14 (5.5)	11 (13.3)	3 (1.8)	.001

Abbreviations: COVID-19, coronavirus disease 2019; ICU, intensive care unit.

[a]Data is presented as n (%) and median [interquartile range] unless specified otherwise.

[b]Disease severity was defined by the seven-category ordinal scale consisting of the following categories: 2, not hospitalized, but unable to resume normal activities; 3, hospitalized, not requiring supplemental oxygen; 4, hospitalized, requiring supplemental oxygen; 5, hospitalized, requiring nasal high-flow oxygen therapy, noninvasive mechanical ventilation, or both; 6, hospitalized, requiring ECMO, invasive mechanical ventilation, or both; or 7, death).

[c]Nine patients were excluded as evaluation of data preceded 30-day readmission date.

[d]Repeat electrocardiograms were not performed in 128 patients (26 non-survivors and 102 survivors) and were excluded from analysis.

[e]33 patients (13 non-survivors and 20 survivors) were excluded as they were on hemodialysis at baseline and/or if serum creatinine was not repeated to assess for renal failure and were excluded from analysis.

[f]31 patients (12 non-survivors and 19 survivors) were excluded as they were on hemodialysis at baseline and were excluded from analysis.

literature.[5,6,9,10,15,19] Septic shock is commonly seen in patients with COVID-19 infection and seen in up to 70% of nonsurvivors based on data from China[21] and United States.[7,9,10] Not surprisingly, patients who were initiated on vasopressors in our study were also found to be at a higher risk for in-hospital mortality.

The findings in our post hoc analysis provides some explanation why patients who were transferred from long-term care facilities were at increased risk for mortality in our study and the study by Rosenthal et al.[10] In our post hoc analysis, we found patients from long-term care facilities had a higher prevalence of coronary artery disease and advanced age (Table S1), which we previously identified as independent risk factors for in-hospital mortality (Table 3). In addition, patients presenting from a long-term care facility had a higher prevalence of hypertension and chronic respiratory disease.

Although we previously did not find these comorbidities to be independent risk factors for mortality (Table 3), these were found to be significant mortality risk factors in previous literature.[6,9,10]

Among the COVID-19 nonsurvivors who were admitted to TBHC during the first month and a half of the city's outbreak, the majority were men over the age of 65 with hypertension and diabetes, one-third were obese, and more than half required supplemental oxygen upon presentation. These findings correspond with previous literature reporting the demographics of patients with COVID-19 in NYC.[7–9] Interestingly, we did not find hypertension as a risk factor for mortality as compared to previous international reports.[6,17,18] Furthermore, we did not identify any comorbidities as independent risk factors for in-hospital mortality by multivariate logistic regression. This was consistent with the findings by Zhou et al.,[5] but not with multiple findings in the United States and specifically NYC.[9,10] In our patient cohort, objective findings were similar compared with previous literature, with the exception of total bilirubin.[5] Disease severity at baseline and at Day 7 were comparable to literature in China, and nonsurvivors had a higher prevalence of invasive mechanical ventilation.[7,11] Chest imaging was positive in nearly 90% of the patient population, which is consistent with previous reports.[22,23]

Hydroxychloroquine (HCQ) and remdesivir have shown activity against SARS-CoV-2 in vitro[24,25]; however, HCQ was administered in approximately 95% of the patients in our study with no patients receiving remdesivir as the primary antiviral agent. Three studies reported higher usage of remdesivir, although it is important to note that none exceeded 10% of their patient population.[7,9,10] This observation could be due to insufficient evidence at the time of the study period to issue recommendations per numerous guidelines which impacted physician prescribing habits to determine which antiviral agent would be optimal.[26,27] In addition, another reason for the increased use of hydroxychloroquine in our study, compared with previous US and NYC studies,[7–10] was due to the lack of randomized controlled trials that were available during the inclusion period, March 1st 2020 to April 15th 2020, with limited access to only nonpeer-reviewed literature.[28] In addition, the first published peer-review literature for the compassionate use of remdesivir in severe COVID-19 was released on April, 10th 2020,[29] and the Emergency Use Authorization of remdesivir was not implemented until May 1st, 2020.[30] These actions led to a shift of increased use of remdesivir for patients with COVID-19 in NYC as the limitations of access to remdesivir and delay of SARS-CoV-2 testing results diminished. However, due to our study period of March 1st, 2020 to April 15th, 2020, a majority of the patients included were initiated on hydroxychloroquine monotherapy or the combination of hydroxychloroquine and azithromycin.

This study, however, has several limitations. First, our study is single-centered as TBHC is a community teaching hospital in Brooklyn, New York that is not part of a larger healthcare system. Our findings are representative of patients from the Brooklyn community, although we recognize that they may not be generalizable to patients from other parts of NYC or outside the NYC area.

Second, as the evaluation of outcomes were halted at a specific date, nine patients in the survivor group were excluded from analysis of 30-readmission. Third, the inclusion period of the study was approximately one and a half months during the COVID-19 pandemic, thus minimizing the potential sample size to evaluate a more accurate assessment of risk factors for mortality in COVID-19 patients. Fourth, data reported elsewhere have correlated elevated interleukin-6 levels[9] and D-dimer with more severe clinical COVID-19 illness.[5,9] Unfortunately, interleukin-6 levels are not performed at our institution, limiting our ability to compare to these studies. In addition, D-dimer was not included in multivariate logistic regression analysis as this baseline parameter was not available for the majority of the patient cohort which would limit the representation of risk for in-hospital mortality. Lastly, even though our study evaluated more variables than previous studies,[5,9] we were unable to assess other potential novel findings due to the risk for overfitting.[14]

In conclusion, risk factors associated with mortality for patients with COVID-19 in a NYC community teaching hospital include advanced age, presentation from nursing home or assisted living facility, initiation of vasopressor therapy, development of renal failure, and elevated total bilirubin. We hope our findings and other emerging data will contribute to the development of an international risk stratification tool in hospitalized patients with COVID-19.

CONFLICT OF INTERESTS

All the authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTIONS

Karina Muzykovsky, James Truong, and Justin A. Andrade had full access to all data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. *Concept and design*: Karina Muzykovsky and James Truong. *Acquisition, analysis, or interpretation of data*: Karina Muzykovsky, James Truong, and Justin A. Andrade. *Drafting of the manuscript*: Karina Muzykovsky, James Truong, and Justin A. Andrade. *Critical Revisions of manuscript for important intellectual content*: Karina Muzykovsky, James Truong, and Justin A. Andrade

PEER REVIEW

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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