Clinical Characteristics, Respiratory Mechanics, and Outcomes in Critically Ill Individuals With COVID-19 Infection in an Underserved Urban Population

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BACKGROUND: The COVID-19 outbreak in the United States has disproportionately affected Black individuals, but little is known about the factors that underlie this observation. Herein, we describe these associations with mortality in a largely minority underserved population. METHODS: This single-center retrospective observational study included all adult subjects with laboratory-confirmed SARS-Cov-2 treated in our ICU between March 15 and May 10, 2020. RESULTS: 128 critically ill adult subjects were included in the study (median age 68 y [interquartile range 61–76], 45% female, and 64% Black); 124 (97%) required intubation. Eighty (63%) subjects died during their in-patient stay, which did not differ by race/ethnicity. Compared with other racial/ethnic groups, Blacks had a greater proportion of women (52% vs 30%, $P = .02$) and subjects with hypertension (91% vs 78%, $P = .035$). Asthma ($P = .03$) was associated with lower in-patient death, primarily among Black subjects ($P = .02$). Among Black subjects, increased age (odds ratio 1.06 [95% CI 1.05–1.22] per year), positive fluid balance (odds ratio 1.06 [95% CI 1.01–1.11] per 100 mL), and treatment with tocilizumab (odds ratio 25.0 [95% CI 3.5–180]) were independently associated with in-patient death, while higher platelets (odds ratio 0.65 [95% CI 0.47–0.89] per 50×10^3/mL) and treatment with intermediate dose anticoagulants (odds ratio 0.08 [95% CI 0.02–0.43]) were protective. Among other race/ethnic groups, higher total bilirubin (odds ratio 1.75 [95% CI 0.94–3.25] per 0.2 mg/dL) and higher maximum lactate (odds ratio 1.43 [95% CI 0.96–2.13] per mmol/L) were marginally associated with increased death, while tocilizumab treatment was marginally protective (odds ratio 0.24 [95% CI 0.05–1.25]). During first 72 h of ventilation, those who died had less increase in P_{aO_2}/F_{IO_2} ($P = .046$) and less reduction in PEEP ($P = .01$) and F_{IO_2} requirement ($P = .002$); these patterns did not differ by race/ethnicity. CONCLUSIONS: Black and other race/ethnicity subjects had similar mortality rates due to COVID-19 but differed in factors that were associated with increased risk of death. In both groups, subjects who died were older, had a positive fluid balance, and less improvement in P_{aO_2}/F_{IO_2}, PEEP, and F_{IO_2} requirement on ventilation. *Key words: COVID-19; coronavirus; outcomes.* [Respir Care 2021;66(6):897–908. © 2021 Daedalus Enterprises]

Introduction

In December 2019, Wuhan Province in China reported an alarming number of cases presenting with respiratory illness that was caused by a novel coronavirus subsequently named SARS-CoV-2.[1,2] The clinical manifestation of infection by this virus is known as coronavirus disease 2019 (COVID-19), and as of this writing has resulted in > 28 million cases in the United States and > 500,000 deaths, with Black individuals representing a significant portion of the observed morbidity and mortality (55 deaths per 100,000).[3,4]

Significantly increased risk of death has been reported in the elderly, in those with prior comorbid conditions,[5,6] and in patients requiring management in the ICU and mechanical ventilation.[3] Despite concentrated efforts in obtaining novel therapeutic possibilities for these patients, the vast majority of trials have failed to conclusively demonstrate improved outcomes secondary to pharmaceutical interventions, though clinical variables and ventilatory support have

been shown to have prognostic and possibly therapeutic value.[5,6]

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COVID-19 has disproportionately affected the Black community in the United States.[4] As of July 10, 2020, demographic data collected by the Centers for Disease Control and Prevention (CDC) from > 250 hospitals in the COVID-19-associated Hospitalization Surveillance Network for the week ending in June 27, 2020, 32.5% of the hospitalized subjects were Black.[3] Furthermore, data from the CDC indicate that 23% of reported deaths in the United States are Black, compared with 17% Black in the general population (weighted population distribution taking into account where deaths occurred), and the rate is more than twice that of whites (55 deaths per 100,000 versus 23 deaths per 100,000).[4] Whether there are racial/ethnic differences in risk factors for death or response to treatment for COVID-19, however, is not well understood.

In this study we report on the clinical characteristics of a largely underserved, racially/ethnically diverse population in a large urban center on the East Coast of the United States and present key clinical and ventilatory characteristics associated with improved outcomes in our population.

QUICK LOOK

Current knowledge

COVID-19 is a highly inflammatory viral disease and since the start of the pandemic data has shown that the outcomes in Black and underserved populations is poor. There have been clinical and epidemiological research in China, European countries and USA that have described this clinical entity but little is known of its effect on the Black population.

What This Paper contributed to Our Knowledge

In our cohort of predominantly Black subjects, we found out that the mortality was high in patients who are on mechanical ventilation, elderly patients with comorbid conditions, and a positive fluid balance 48 h post intubation. We did not find any differences in outcomes by race, although there was a slightly higher mortality in Black individuals.

Methods

This is a single-center retrospective case series of all ICU subjects admitted to the hospital who were diagnosed with COVID-19. The study was carried out at a 700-bed, tertiary care, academic medical center with a 28-bed medical ICU and a surge capacity of 60 ICU beds during the COVID-19 pandemic. Subjects from both medical and surgical ICUs were included. The hospital primarily serves the neighboring communities with a culturally and ethnically diverse population of 59% Black, 23% Hispanic, 12% white, and 4% Asian. Almost half of the adults (45.1%) had a family income of ≤ $26,200, and 68% had a family income of ≤ $50,800. More than 80% of discharges are covered by Medicare/Medicaid. We studied all adult subjects with a confirmed SARS-CoV-2 polymerase chain reaction test who were treated in the ICU between March 15 and May 10, 2020. During this surge period, we only admitted patients to the ICU if they required intubation, while the patients on high-flow nasal cannula or CPAP were managed on the step-down unit by our pulmonologists. Patients with incomplete data in terms of the main clinical outcomes and demographics were excluded from the study. The study was approved by the hospital institutional review board, who deemed it to be low risk and waived the requirement for informed consent. Data were collected from the electronic medical records using International Classification of Disease 9–10 codes. Subjects who presented with characteristic symptoms were tested for COVID-19. A total of 673 subjects were admitted to our hospital with confirmed COVID infection; of these subjects, 128 were managed in the ICU during this time. We collected demographic data, presenting comorbidities, laboratory values and novel therapies used for COVID-19, and mortality and hospital discharge data from the medical record. Respiratory and hemodynamic values were collected at baseline and at 24, 48, and 72 h.

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Statistical Analysis

Clinical and demographic data were evaluated relative to the primary end point, in-patient death, overall, and by race/ethnicity (Black versus white/Hispanic/other). Unadjusted medians with interquartile ranges (IQR) were obtained with non-parametric Kruskal-Wallis tests, while number (percent) were obtained using chi-square or Fisher exact tests, as appropriate. Multivariable logistic regression was conducted to determine independent associations of clinical, demographic, and treatment variables with in-patient death, testing any variable with unadjusted $P \leq .20$ and with data available for at least 80% of subjects; elimination of variables was conducted sequentially by eliminating the least significant terms or most unstable odds ratio estimates.

Longitudinal changes in respiratory parameters during the first 72 h of ventilation were tested using mixed modeling, accounting for correlated measurements within person. All models of respiratory parameters were adjusted for age, race, sex, body mass index, and total days on the ventilator, with the main discriminating variables being time (0, 24, 48, or 72 h after intubation) and in-patient death versus survival. Linear trends were tested using time as a continuous variable. Interactions of in-patient death or Black race with time were also used to test for differences in change in respiration parameters over time by race and outcome. For all analyses, significant values are reported if $P < .05$ or if inclusion of a term in the model improved model fit, using reductions in –2 log-likelihood values ≥ 4 as evidence of a better fitting model.

Results

One hundred twenty-eight subjects with laboratory-confirmed COVID-19 were admitted to the ICU. Intubation was deemed necessary in 124 (97%) subjects. Demographic and clinical characteristics are summarized in Table 1. Median age was 68 y (IQR 61–75.5], and 57 (45%) were female. Blacks represented 64% of the population and had a likelihood of survival of 35% in comparison to 41% of the remaining population; this difference was not statistically significant ($P = .57$). Overall, 83 (63%) subjects died while admitted. Subjects who died in the hospital were a median of 6 y older than those who did not (median age 64 vs 70, $P = .02$); this was statistically significant only in Black subjects ($P = .006$).

Nearly all subjects had bilateral infiltrates upon admission (96%; Table 1). Cardiovascular comorbidities were extremely common (88%), particularly hypertension (87%), followed by diabetes (57%) and respiratory comorbidities (32%). Two or more comorbidities were seen in 78% of subjects. Despite a high proportion of subjects with history of hypertension, diabetes, and coronary artery disease, only 38% of subjects were being treated with renin angiotensin aldosterone system inhibition (angiotensin-converting enzyme inhibitors and angiotensin receptor blockers) prior to admission. Of the comorbidities, only respiratory, particularly asthma, were negatively associated with in-patient death; respiratory comorbidities were present in 44% of subjects discharged alive versus 25% of in-patients who died ($P = .033$), and asthma was present in 15% of subjects discharged alive versus 3% of in-patients who died ($P = .03$). Asthma was associated to a greater extent in Blacks who were discharged alive (21% vs 4%, $P = .02$), whereas overall respiratory comorbidities were more prevalent in other race/ethnicity groups discharged alive (42% vs 15%, $P = .049$). Medication use did not differ by in-patient death.

Laboratory parameters associated with in-patient death included higher procalcitonin ($P = .01$), higher creatinine ($P = .004$), lower fibrinogen ($P = .003$), lower platelets ($P = .03$), and longer partial thromboplastin time ($P = .009$), along with marginally higher alkaline phosphatase ($P = .051$) (Table 2). These differed somewhat by race/ethnicity. Among Black subjects, only lower fibrinogen was significantly associated with in-patient death ($P = .02$), with higher procalcitonin ($P = .08$), lower platelets ($P = .057$), and lower lactate dehydrogenase ($P = .09$) marginally associated. More admission laboratory values were associated with in-patient death among white/Hispanic/other subjects: higher lactate ($P = .02$), higher creatinine ($P = .003$), higher direct bilirubin ($P = .005$), higher total bilirubin ($P = .006$), higher lactate dehydrogenase ($P = .005$), higher procalcitonin ($P = .02$), and higher partial thromboplastin time ($P = .033$). Considering maximum values recorded during the hospitalization, in-patient death was associated with higher lactate ($P < .001$, significant in both race/ethnic groups), higher ferritin ($P = .02$, significant in Black subjects only), higher procalcitonin ($P = .001$, significant in both race/ethnic groups), lower fibrinogen ($P = .009$, significant in Black subjects only), and higher creatinine ($P = .02$ for maximum within the first week, significant in white/Hispanic/other group only). Maximum C-reactive protein was also marginally higher for those with in-patient death ($P = .07$, in Black subjects only).

Table 3 presents the treatments and clinical outcomes and associations with in-patient death. Several medications were administered to these subjects, with the most common being anticoagulants (98%), tocilizumab (71%), and hydroxychloroquine (66%). Of all medications noted, only steroids were associated with better outcomes (44% among all patients discharged alive vs 26% in those with in-patient death, $P = .041$), but this association was not significant in either race/ethnic group. Conversely, treatment with remdesivir was associated with improved outcomes in white/Hispanic/other subjects ($P = .01$) but not Black subjects ($P > .99$).

Table 1. Associations of Admission Characteristics of ICU Subjects With COVID-19 With Outcomes by Race/Ethnicity

	Overall	All Subjects			Black			White/Hispanic/Other		
		Discharged Alive	In-Hospital Death	*P*	Discharged Alive	In-Hospital Death	*P*	Discharged Alive	In-Hospital Death	*P*
Subjects	128	48 (38)	80 (63)		29 (35)	53 (65)		19 (41)	27 (59)	
Age, y	68 (61–75.5)	64 (58–73.5)	70 (63–77.5)	.02	63 (57–70)	69 (64–74)	.006	70 (61–77)	74 (61–84)	.25
Female	57 (45)	23 (48)	34 (43)	.59	16 (55)	27 (51)	.82	7 (37)	7 (26)	.52
Race/ethnicity				.10			NA			.067
African-American	82 (64)	29 (60)	53 (66)		NA	NA				
White	6 (5)	4 (8)	2 (3)		NA	NA		4 (21)	2 (7)	
Hispanic	16 (13)	9 (19)	7 (9)		NA	NA		9 (47)	7 (26)	
Other	24 (19)	6 (13)	18 (23)		NA	NA		6 (32)	18 (67)	
BMI, kg/m^2	29.5 (24.5–35.5)	30 (25.5–37.5)	28 (23–35)	.21	32 (28–38)	30 (26–36)	.24	27 (25–32)	25 (22–33)	.29
Bilateral infiltrates	121 (96)	47 (98)	74 (95)	.65	28 (96)	50 (96)	> .99	19 (100)	24 (92)	.50
Comorbidities										
Respiratory	41 (32)	21 (44)	20 (25)	.033	13 (45)	16 (30)	.23	8 (42)	4 (15)	.049
COPD	22 (17)	10 (21)	12 (15)	.47	5 (17)	11 (21)	.78	5 (26)	1 (4)	.068
Asthma	9 (7)	7 (15)	2 (3)	.03	6 (21)	2 (4)	.02	1 (5)	0 (0)	.41
Obstructive sleep apnea	16 (13)	8 (17)	8 (10)	.28	5 (17)	5 (9)	.31	3 (16)	3 (11)	.68
Cardiovascular	113 (88)	43 (90)	70 (88)	.78	26 (90)	49 (92)	.69	17 (89)	21 (78)	.44
Heart failure	27 (21)	8 (17)	19 (24)	.38	4 (14)	12 (23)	.40	4 (21)	7 (26)	> .99
Atrial fibrillation	15 (12)	5 (10)	10 (13)	.78	3 (10)	5 (9)	> .99	2 (11)	5 (19)	.68
Coronary artery disease	31 (24)	12 (25)	19 (24)	> .99	6 (21)	13 (25)	.79	6 (31)	6 (22)	.51
Hypertension	111 (87)	42 (88)	69 (86)	> .99	26 (90)	49 (92)	.69	16 (84)	20 (74)	.49
Liver	5 (4)	1 (2)	4 (5)	.65	0 (0)	2 (4)	.54	1 (5)	2 (7)	> .99
Cirrhosis	5 (4)	1 (2)	4 (5)	.65	0 (0)	2 (4)	.54	1 (5)	2 (7)	> .99
Liver transplant	2 (2)	1 (2)	1 (1)	>.99	0 (0)	1 (2)	> .99	1 (5)	0 (0)	.41
Renal	35 (27)	10 (21)	25 (31)	.23	7 (24)	16 (30)	.62	3 (16)	9 (33)	.31
Chronic kidney disease	26 (20)	7 (15)	19 (24)	.26	5 (17)	11 (21)	.78	2 (11)	8 (30)	.16
ESRD on dialysis	11 (9)	3 (6)	8 (10)	.53	2 (7)	7 (13)	.48	1 (5)	1 (4)	> .99
Kidney transplant	2 (2)	0 (0)	2 (3)	.53	0 (0)	1 (2)	> .99	0 (0)	1 (4)	> .99
Other	74 (58)	28 (58)	46 (57)	> .99	19 (66)	32 (60)	.81	9 (47)	14 (52)	> .99
Diabetes	73 (57)	28 (58)	45 (56)	.86	19 (66)	31 (58)	.64	9 (47)	14 (52)	> .99
HIV	2 (2)	0 (0)	2 (3)	.53	0 (0)	2 (4)	.54	0 (0)	0 (0)	NA
Comorbidities, no.				.23			.34			.43
0	6 (5)	0 (0)	6 (8)		0 (0)	3 (6)		0 (0)	3 (11)	
1	22 (17)	9 (19)	13 (16)		3 (10)	9 (17)		6 (32)	4 (15)	
2	39 (30)	18 (38)	21 (26)		12 (41)	14 (26)		6 (32)	7 (26)	
3	28 (22)	11 (23)	17 (21)		8 (28)	10 (19)		3 (16)	7 (26)	
4+	33 (26)	10 (21)	23 (29)		6 (21)	17 (32)		4 (21)	6 (22)	
Medications at admission										
Antiplatelets	60 (47)	21 (44)	39 (49)	.58	14 (48)	28 (53)	.82	7 (37)	11 (41)	> .99
NSAIDs	8 (6)	3 (6)	5 (6)	> .99	3 (10)	6 (9)	> .99	0 (0)	0 (0)	NA
ACEi/ARB	49 (38)	22 (46)	27 (34)	.17	13 (45)	21 (40)	.81	9 (47)	6 (22)	.11

(Continued)

Table 1. Continued

	Overall	All Subjects			Black			White/Hispanic/Other		
		Discharged Alive	In-Hospital Death	*P*	Discharged Alive	In-Hospital Death	*P*	Discharged Alive	In-Hospital Death	*P*
Novel anticoagulants	13 (10)	5 (10)	8 (10)	.94	1 (3)	4 (8)	.65	4 (21)	4 (15)	.70
Heparin	7 (5)	3 (6)	4 (5)	.76	3 (10)	3 (6)	.66	0 (0)	1 (4)	> .99
Statins	74 (58)	30 (63)	44 (55)	.41	17 (59)	31 (58)	> .99	13 (68)	13 (48)	.23
Prednisone	8 (6)	3 (6)	5 (6)	> .99	2 (7)	4 (8)	> .99	1 (5)	1 (4)	> .99
Medications, no.				.42			.22			.42
0	19 (15)	5 (10)	14 (18)		3 (10)	6 (11)		2 (11)	8 (29)	
1	39 (30)	15 (31)	24 (30)		10 (34)	17 (32)		5 (26)	7 (26)	
2	39 (30)	17 (35)	22 (28)		9 (31)	13 (25)		8 (42)	9 (33)	
3	22 (17)	6 (13)	16 (20)		3 (10)	15 (28)		3 (16)	1 (4)	
4	9 (7)	5 (10)	4 (5)		4 (14)	2 (4)		1 (5)	2 (7)	

Data are presented as *n* (%) or median (interquartile range).
BMI = body mass index
NA = not available
ESRD = end-stage renal disease
HIV = human immunodeficiency virus
NSAID = nonsteroidal anti-inflammatory drug
ACEi/ARB = angiotensin-converting enzyme inhibitors and angiotensin receptor blockers

Figure 1 presents longitudinal respiratory parameters for subjects during the first 72 h of ventilation, adjusting for age, sex, race, body mass index, and total days on the ventilator. P_{aO_2}/F_{IO_2} generally increased over time ($P < .001$) but increased earlier and to a greater degree in those discharged alive ($P = .046$). Similarly, F_{IO_2} requirements ($P < .001$) decreased significantly over time but decreased earlier and more in those discharged alive ($P = .002$). PEEP decreased only in surviving subjects ($P = .03$), while plateau pressure decreased significantly for all subjects ($P = .008$) but did not differ by outcome. Mean arterial pressure and compliance did not change materially during ventilation, as shown in Figure 2. None of the respiratory or ventilation parameters differed by race/ethnicity (data not shown). As shown in Table 3, positive fluid balance in the first 48 h of intubation was also significantly associated with greater mortality ($P = .007$) but was significant only in Black subjects ($P = .01$).

The full respiratory parameters at admission and at intubation are presented in Table 4. At admission, oxygen interface was predominantly either nasal cannula (54%) or nonrebreathing mask (36%), with marginal difference by in-patient death ($P = .054$). Those subjects with in-hospital death presented with higher oxygen requirements at admission and prior to intubation. On intubation, the median P_{aO_2}/F_{IO_2} was 63 (IQR 50–105), PEEP was 10 cm H_2O (IQR 7–10), plateau pressure was 25 cm H_2O (IQR 22–30), and compliance was 26 mL/cm H_2O (IQR 21–33) (Table 4). None of these values were significantly different between survivors and in-patient deaths. Early intubation (defined as within the first 2 d of hospitalization), prone positioning, airway pressure release ventilation, and vasodilator therapy were not associated with in-patient death. Extubation was successful in 35 subjects (29%), of whom 31 (89%) were subsequently discharged alive ($P < .001$).

Because of differences in patient profiles by race/ethnicity group, logistic regression models were developed separately by race, testing variables with unadjusted $P \leq .20$ (Fig. 3). Among Black subjects, higher age (odds ratio [OR] 1.13 [95% CI 1.05–1.22] per additional year of age, $P = .002$), positive fluid balance (OR 1.06 [95% CI 1.02–1.11] per 100 mL, $P = .008$), and tocilizumab treatment (OR 25 [95% CI 3.5–180]) were independently associated with risk of in-patient death, while a higher platelet count (OR 0.65 [95% CI 0.47–0.89] per 50,000/mL, $P = .008$), and intermediate dose anticoagulation (OR 0.08 [95% CI 0.02–0.43]) were associated with improved outcomes. Among white/Hispanic/other subjects, marginally associated risk factors included higher total bilirubin at admission (OR 1.75 [95% CI 0.93–3.25], $P = .08$) and higher maximum lactate (OR 1.43 [95% CI 0.96–2.13], $P = .08$), while tocilizumab treatment was marginally

Table 2. Laboratory Parameters of ICU Subjects With COVID-19 and Associations With In-Patient Death by Race/Ethnicity

	Overall	All Subjects			Black			White/Hispanic/Other		
		Discharged Alive	In-Hospital Death	*P*	Discharged Alive	In-Hospital Death	*P*	Discharged Alive	In-Hospital Death	*P*
Admission laboratory parameters										
Alkaline phosphatase, IU/L	82 (67–115)	78 (65–92)	85 (72–131)	.051	78 (61–97)	82.5 (72.5–114)	.13	78 (65–92)	96.5 (72–157)	.14
Alanine aminotransferase, IU/L	27 (18–49)	26.5 (18–42)	31.5 (18–52)	.49	26 (18–42)	25.5 (16–48.5)	.85	30 (13–42)	42 (20–59)	.11
Aspartate aminotransferase, IU/L	45.5 (29.5–74)	43 (32–54)	46 (29–81)	.24	37 (32–71)	46 (28.5–77.5)	.71	49 (27–54)	53 (31–88)	.14
White blood cell count, $10^3/\mu L$	8,380 (6,155–12,945)	8,995 (6,560–13,145)	8,170 (5,875–12,615)	.51	10,120 (7,010–13,060)	7,880 (5,720–12,400)	.30	8,570 (5,220–13,230)	8,930 (6,190–12,830)	.88
Neutrophil, %	80.1 (70.8–84.9)	78.8 (70.6–85.2)	80.5 (70.8–84.9)	.60	75.5 (62.9–84.5)	80.6 (69.0–85.0)	.23	81.8 (73,7–86.8)	80.5 (78.0–84.4)	.48
Lymphocyte, %	9.8 (6.5–15.9)	8.65 (6.5–16.1)	10.1 (6.3–15.9)	.65	8.5 (7.0–16.7)	10.8 (7.4–16.1)	.60	8.8 (6.1–15.1)	9.3 (5.3–12.6)	.96
Bands, %	0 (0–2.6)	0 (0–1)	0 (0–6)	.35	0 (0–3.1)	0 (0–3.1)	.88	0 (0–0)	0 (0–12.5)	.07
Troponin, ng/mL	0.04 (0.02–0.12)	0.04 (0.01–0.12)	0.04 (0.02–0.15)	.21	0.04 (0.01–0.14)	0.04 (0.02–0.12)	.73	0.04 (0.01–0.07)	0.05 (0.03–0.28)	.15
Lactate, mmol/L	1.80 (1.29–3.00)	1.80 (1.20–2.40)	1.82 (1.33–3.28)	.14	1.87 (1.41–2.50)	1.8 (1.2–3.2)	.90	1.32 (1.10–2.24)	2.2 (1.5–4.6)	.02
Serum sodium, mmol/L	138 (136–143)	138 (136–140)	138 (135–145)	.32	138 (136–139)	138 (136–143)	.50	138 (136–140)	140 (132–149)	.43
Creatinine, mg/dL	1.45 (1.0–2.45)	1.1 (0.8–1.75)	1.6 (1.1–2.75)	.004	1.2 (0.9–2.2)	1.5 (1.0–2.5)	.18	1.1 (0.7–1.7)	2.0 (1.4–2.8)	.003
Bilirubin, direct, mg/dL	0.3 (0.2–0.5)	0.3 (0.2,0.5)	0.3 (0.2–0.5)	.22	0.3 (0.2–0.5)	0.3 (0.2–0.4)	.61	0.2 (0.2–0.4)	0.45 (0.3–0.6)	.005
Bilirubin, total, mg/dL	0.5 (0.4–0.8)	0.5 (0.3–0.8)	0.5 (0.4–0.8)	.36	0.5 (0.3–0.9)	0.5 (0.3–0.65)	.43	0.4 (0.3–0.7)	0.75 (0.5–1.1)	.006
Ferritin, ng/mL	988 (491–2,181)	798 (430–1,744)	1,034 (500–2,767)	.15	693 (429–1,765)	1,005 (481–1,944)	.49	941 (464–1,723)	1,442 (798–3,450)	.11
D-dimer, ng/mL	2,700 (1,400–5,860)	2,550 (1,160–4,460)	2,805 (1,415–5,945)	.33	2,825 (1,630–4,225)	2,650 (1,300–6,030)	.96	1,670 (630–5,950)	3,210 (2,140–5,520)	.14
C-reactive protein, mg/L	178 (100–262)	161 (90–248)	184 (113–272)	.32	144 (94–239)	192 (109–277)	.23	162 (84–248)	177 (120–223)	.95
Lactate dehydrogenase, IU/L	499 (381–653)	464 (361–686)	506 (404–642)	.65	592 (428–752)	500 (386–648)	.09	364 (272–502)	514 (439–601)	.005
Procalcitonin, ng/mL	0.55 (0.20–2.14)	0.37 (0.11–0.99)	0.90 (0.22–5.87)	.01	0.31 (0.11–0.82)	0.61 (0.18–2.48)	.08	0.46 (0.25–0.99)	1.93 (0.51–11.2)	.02
Prothrombin time, s	15.1 (13.9–16.7)	15.1 (13.9–16.0)	15.1 (13.9–16.9)	.51	15.1 (14.3–15.5)	14.7 (13.8–16.4)	.79	14.9 (13.5–18.5)	15.8 (14.6–18.2)	.15
Partial thromboplastin time, s	36.6 (31.5–46.3)	33.5 (30.0–41.4)	37.8 (33.6–48.5)	.009	34.0 (29.7–40.7)	36.7 (33.1–48.1)	.12	33.5 (30.1–43.0)	42.5 (37.1–60.4)	.033
International normalized ratio	1.2 (1.0–1.3)	1.2 (1.0 1.2)	1.2 (1.0–1.3)	.86	1.2 (1.1–1.2)	1.1 (1.0–1.3)	.57	1.2 (1.0–1.5)	1.2 (1.1–1.5)	.28
Platelets, $10^3/\mu L$	196 (151–271)	229 (165–266)	180 (141–278)	.033	225 (168–299)	180 (140–275)	.057	231 (155–263)	180 (147–280)	.26
Fibrinogen, mg/dL	570 (490–675)	636 (568–774)	544 (465–635)	.003	638 (570–768)	555 (490–645)	.02	627 (566–793)	503 (386–583)	.066
Maximum laboratory parameters										
Lactate, mmol/L	2.8 (1.8–5.9)	2.00 (1.45–3.00)	3.82 (2.18–7.72)	< .001	2.3 (1.6–3.1)	3.2 (2.0–6.9)	.01	1.9 (1.4–2.6)	5.1 (2.9–10.1)	.002
Ferritin, ng/mL	2,340 (824–4,785)	1,647 (670–3,237)	2,707 (1,051–8,704)	.02	1,503 (655–3,084)	2,650 (1,022–9,219)	.038	2,340 (824–3,237)	2,922 (1,068–5,392)	.21
D-dimer, ng/mL*	7,690 (3,550–23,000)	5,575 (2,815–19,300)	9,430 (3,940–25,000)	.20	6,560 (3,970–25,000)	11,680 (3,370–25,000)	.76	4,520 (1,870–13,380)	7,520 (4,050–14,150)	.13
C-reactive protein, mg/L	223 (161–304)	193 (151–274)	238 (168–327)	.07	189 (144–270)	253 (10–332)	.062	213 (161–285)	211 (161–279)	.79
Lactate dehydrogenase, IU/L	702 (537–1,027)	655 (502–915)	726 (549–1,048)	.17	705 (558–962)	780 (563–1,165)	.58	616 (375–748)	649 (546–861)	.14
Procalcitonin, ng/mL	1.21 (0.30–10.08)	0.49 (0.15–2.02)	2.04 (0.47–11.4)	.001	0.42 (0.12–2.46)	1.4 (0.4–10.4)	.01	0.62 (0.25–2.02)	4.48 (1.24–15.83)	.02
Fibrinogen, mg/dL	642 (536–730)	681 (638–784)	603 (510–700)	.009	697 (638–784)	609 (527–709)	.033	679 (536–793)	602 (468–668)	.09
Creatinine, mg/dL	2.5 (1.4–4.6)	1.7 (1.2–4.2)	2.8 (1.9–4.9)	.02	1.8 (1.1–4.0)	2.8 (1.5–4.3)	.20	1.4 (1.2–4.3)	2.8 (2.2–5.4)	.02

Data are presented as *n* (%) or median (interquartile range).

* D-dimer values ≥ 25,000 ng/mL are reported as 25,000 ng/mL, the maximum measurable value.

Table 3. Association of Treatment and Clinical Outcome With In-Patient Death by Race/Ethnicity

	Overall	All Subjects			Black			White/Hispanic/Other		
		Discharged Alive	In-Hospital Death	*P*	Discharged Alive	In-Hospital Death	*P*	Discharged Alive	In-Hospital Death	*P*
Murray score	2.8 (2.3–3.3)	2.8 (2.5–3.3)	2.8 (2.3–3.3)	.73	2.5 (2.3–3.1)	2.8 (2.3–3.0)	.51	3.0 (2.8–3.3)	2.8 (2.0–3.3)	.30
Fluid balance in first 48 h of intubation, mL*	2,509 (835–3,698)	1,773 (–30 to 3,020)	2,676 (1,481–4,255)	.007	1,722 (235–2,862)	2,664 (1,641–4,040)	.01	1,773 (–47 to 3,129)	2,919 (703–5,813)	.18
Positive fluid balance	96 (85)	33 (73)	63 (93)	.007	21 (75)	44 (96)	.02	12 (71)	19 (86)	.26
Medications										
Hydroxychloroquine	84 (66)	30 (63)	54 (68)	.56	21 (72)	37 (70)	> .99	9 (47)	17 (63)	.37
Steroids	42 (33)	21 (44)	21 (26)	.041	14 (48)	16 (30)	.15	7 (37)	5 (19)	.19
Tocilizumab	91 (71)	34 (71)	57 (71)	.96	19 (66)	44 (83)	.10	15 (79)	13 (48)	.064
Paralytics	50 (40)	19 (40)	31 (40)	> .99	12 (43)	23 (45)	> .99	7 (37)	7 (28)	.74
Anticoagulation	126 (98)	48 (100)	78 (98)	.53	29 (100)	53 (100)	> .99	19 (100)	25 (93)	.50
Full dose	84 (66)	32 (67)	52 (65)	.85	17 (59)	37 (70)	.34	15 (79)	15 (56)	.13
Intermediate dose	27 (21)	14 (29)	13 (16)	.08	11 (38)	9 (17)	.058	3 (16)	4 (15)	> .99
Prophylactic dose	70 (55)	26 (54)	44 (55)	.93	17 (59)	34 (64)	.64	9 (47)	10 (37)	.55
Remdesivir	17 (13)	9 (19)	8 (6)	.18	3 (10)	7 (13)	> .99	6 (32)	1 (4)	.01
Convalescent plasma	3 (2)	3 (6)	0 (0)	.051	2 (7)	0 (0)	.12	1 (5)	0 (0)	.41
Clinical treatments										
Prone positioning	44 (35)	19 (40)	25 (32)	.37	13 (46)	19 (37)	.48	6 (32)	6 (23)	.73
Airway pressure release ventilation	5 (4)	2 (4)	3 (4)	> .99	1 (4)	3 (6)	> .99	1 (5)	0 (0)	.42
Tracheostomy	7 (6)	6 (13)	1 (1)	.01	4 (14)	1 (2)	.051	2 (11)	0 (0)	.17
ECMO	6 (5)	5 (11)	1 (1)	.028	3 (11)	1 (2)	.12	2 (11)	0 (0)	.17
Vasodilator therapy	9 (7)	5 (11)	4 (5)	.29	4 (15)	3 (6)	.22	1 (5)	1 (4)	> .99
Clinical outcomes										
Hospital length of stay, d	13 (7–18)	16 (13–22)	11 (6–16)	< .001	16 (10–22)	13 (8–18)	.14	16.5 (15–22)	7 (4–12)	< .001
ICU length of stay, d	7 (4–14)	7 (5–15)	7 (4–13.5)	.47	6.5 (3–15)	10 (5–15)	.40	9.5 (6–18)	5 (2–10)	.02
Days on ventilator*	7 (4–14)	7 (4–15.5)	7 (4–13)	.65	7 (4–15)	10 (5–10)	.51	9 (3–18)	5.5 (2–9)	.09
Days prior to intubation*	2 (0–4)	2 (0–4)	1.8 (0–4)	.98	3 (0–4)	2 (0.5–4)	.67	1.5 (0.25–4)	0.75 (0–3)	.34
Withdrawal of care	49 (38)	1 (2)	48 (60)	< .001	1 (3)	29 (55)	< .001	0 (0)	19 (70)	< .001
Palliative care	77 (60)	18 (38)	59 (74)	< .001	11 (38)	37 (70)	.009	7 (37)	22 (81)	.005
Need for CRRT/HD	35 (27)	10 (21)	25 (31)	.20	6 (21)	18 (34)	.31	4 (21)	7 (26)	> .99
Successful extubation*	35 (29)	31 (70)	4 (5)	< .001	17 (68)	4 (5)	< .001	14 (74)	0 (0)	< .001
Reintubation	6/35 (17)	3/31 (10)	3/4 (75)	.01	2/17 (12)	3/4 (75)	.03	1/14 (7)	0 (0)	> .99

Data are presented as *n* (%) or median (interquartile range).

* Data for fluid balance and intubation/ventilation presented for the 124 subjects requiring intubation.

ECMO = extracorporeal membrane oxygenation

CRRT = continuous renal replacement therapy

HD = hemodialysis

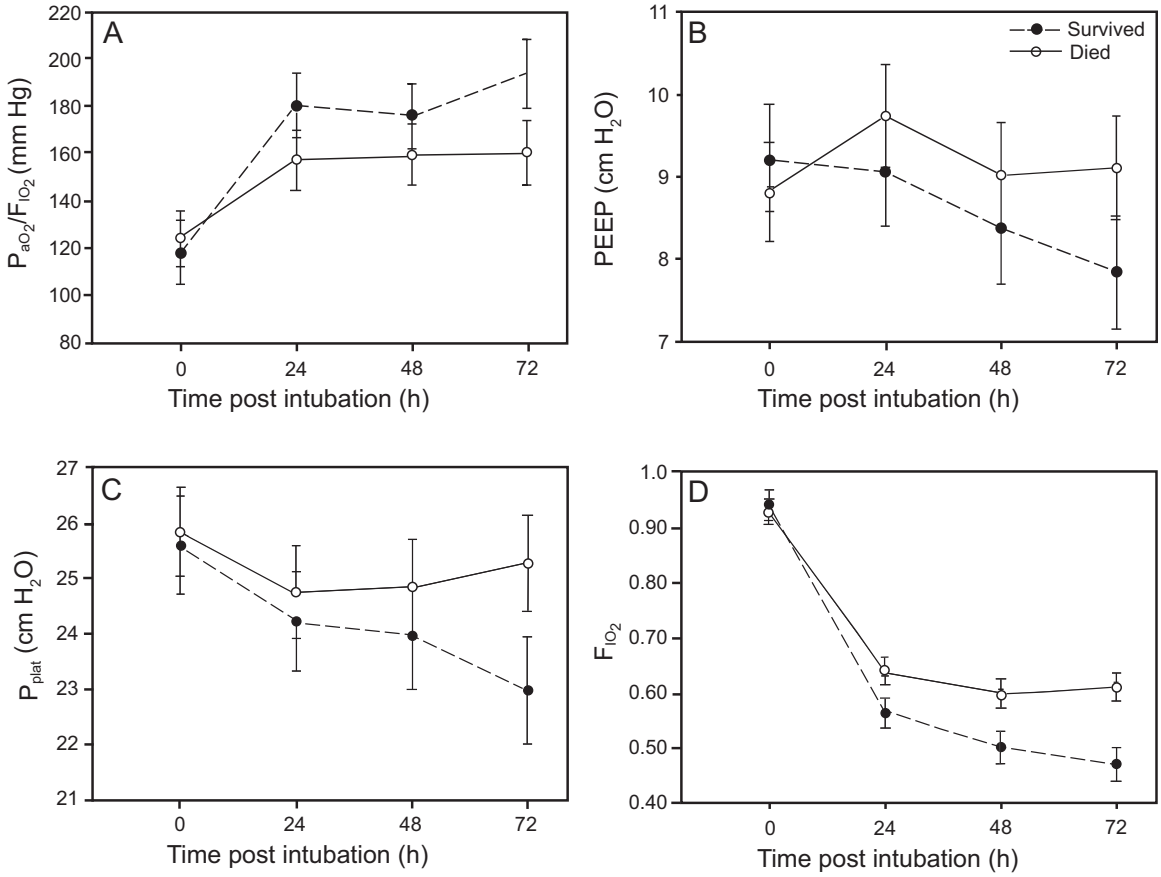

Fig. 1. Longitudinal ventilation parameters associated with in-patient death. Least squares means ± SD presented from mixed models adjusted for race, sex, age, body mass index, and total time on ventilator. (A) P_{aO_2}/F_{IO_2}; (B) PEEP; (C) plateau pressure (P_{plat}); and (D) F_{IO_2} requirement (%).

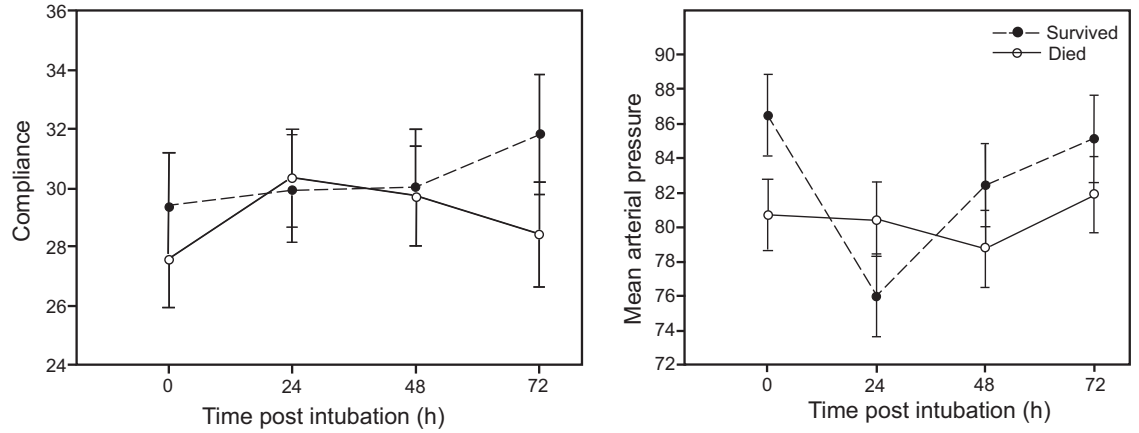

Fig. 2. Longitudinal ventilation parameters not associated with in-patient death. Least squares means ± SD presented from mixed models adjusted for race, sex, age, body mass index, and total time on ventilator. (A) Compliance; (B) mean arterial pressure.

protective (OR 0.24 [95% CI 0.05–1.25], $P = .09$). In sensitivity analyses removing subjects with an ICU length of stay ≤ 2 d, who may not have had an opportunity to receive certain medications or therapies, the model for Blacks remained essentially unchanged, while among white/Hispanic/other race subjects, only higher total bilirubin at admission remained a significant risk factor (OR 1.74 [95% CI 1.04–2.91], $P = .036$).

Table 4. Respiratory Parameters at Admission and Prior to Intubation by In-Patient Death and Race/Ethnicity

	Overall	All Subjects			Black			White/Hispanic/Other		
		Discharged Alive	In-Hospital Death	*P*	Discharged Alive	In-Hospital Death	*P*	Discharged Alive	In-Hospital Death	*P*
At admission/prior to intubation										
Oxygen mode at admission				.054			.030			.21
Room air	5 (5)	1 (2)	4 (6)		0 (0)	2 (4)		1 (5)	2 (9)	
Nasal cannula	63 (54)	25 (54)	38 (54)		16 (59)	33 (69)		9 (47)	5 (22)	
Non-rebreather mask	42 (36)	14 (30)	28 (39)		5 (19)	12 (25)		9 (47)	16 (70)	
Other	7 (6)	6 (13)	1 (1)		6 (22)	1 (2)		0 (0)	0 (0)	
P_{aO_2}/F_{IO_2} at admission	109 (64–174)	134 (79–183)	105 (64–166)	.53	137 (54–183)	117 (74–187)	.80	134 (88–169)	76 (56–104)	.039
P_{aO_2}/F_{IO_2} minimum prior to intubation	62 (48–100)	61 (49–110)	62 (48–89)	.58	55 (48–110)	62 (48–89)	.93	79 (50–133)	64 (49–100)	.50
Need for intubation	124 (97)	47 (98)	77 (96)	> .99	28 (97)	51 (96)	> .99	19 (100)	26 (96)	> .99
Days of mid-flow prior to intubation	1.0 (0.2–2.5)	1.3 (0.5–3.0)	0.5 (0–1.0)	.13	2.0 (0.5–4.0)	0.5 (0.1–2.5)	.08	0.5 (0.25–2.0)	0.5 (0–2.0)	.62
Early intubation	59 (49)	21 (47)	38 (50)	.85	11 (42)	22 (44)	> .99	10 (53)	16 (62)	.76
At or just before start of intubation*										
Oxygen mode				.061			.14			.21
Nasal cannula	19 (16)	6 (14)	13 (18)		3 (12)	9 (18)		3 (16)	4 (17)	
Non-rebreather mask	71 (61)	23 (52)	48 (67)		11 (44)	29 (59)		12 (63)	19 (83)	
High-flow nasal cannula	9 (8)	4 (9)	5 (7)		3 (12)	5 (10)		1 (5)	0 (0)	
CPAP	7 (6)	3 (7)	4 (6)		2 (8)	4 (8)		1 (5)	0 (0)	
Other	10 (9)	8 (18)	2 (3)		6 (24)	2 (4)		2 (11)	0 (0)	
P_{aO_2}/F_{IO_2}	63 (50–105)	79 (50–126)	63 (49–91)	.14	62 (50–116)	62 (48–83)	.38	85 (52–161)	67 (51–105)	.30
Tidal volume, mL	445 (400–475)	450 (380–480)	420 (400–473)	.89	450 (370–500)	400 (400–450)	.72	450 (400–460)	450 (400–500)	.33
PEEP, cm H_2O	10 (7–10)	10 (8–12)	8 (5–10)	.24	10 (8–10)	10 (8–10)	.95	10 (5–14)	8 (5–10)	.055
Compliance, mL/cm H_2O	26 (21–33)	27 (19–34)	26 (22–33)	.61	28 (20–35)	26 (23–31)	.55	25 (18–32)	30 (22–38)	.11
Plateau pressure, cm H_2O	25 (22–30)	25 (22–31)	25 (22–30)	.86	25 (21–32)	26 (23–30)	.64	27 (23–29)	24 (20–32)	.38
Mean arterial pressure, mm Hg	79 (70–92)	82 (72–96)	79 (68–92)	.24	82 (74–94)	78 (70–91)	.28	82 (71–104)	80 (66–94)	.51
P_{aO_2}/F_{IO_2}, %	100 (100–100)	100 (100–100)	100 (97–100)	.08	100 (100–100)	100 (80–100)	.21	100 (100–100)	100 (100–100)	.24

Data are presented as *n* (%) or median (interquartile range).

* Data for intubation parameters presented for the 124 subjects requiring intubation.

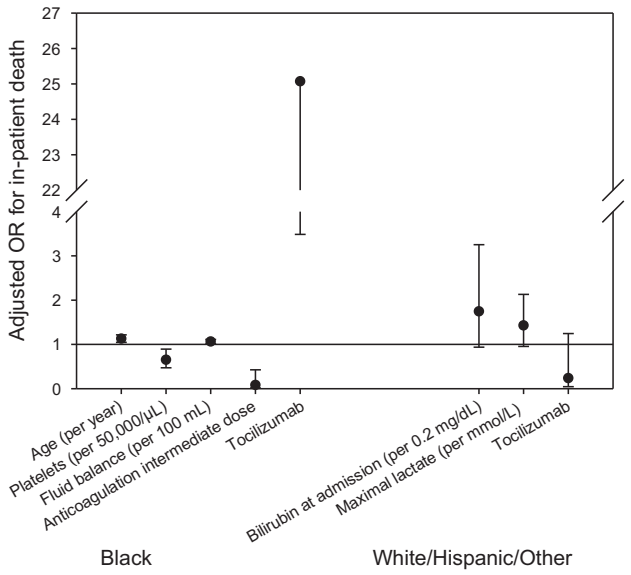

Fig. 3. Odds ratios (95% CI) of factors associated with in-patient death, by race/ethnicity, presented from race/ethnicity-specific adjusted logistic regression models. The upper limit of the 95% CI for tocilizumab treatment in Black subjects is 180 (not shown). OR = odds ratio.

Discussion

In this retrospective case series of critically ill subjects, we evaluated racial/ethnic differences in mortality and risk factors for in-patient death in a diverse, urban ICU. While we observed no statistically significant difference in risk for mortality between Black and white/Hispanic/other subjects, our results revealed different patterns of risk for the 2 race/ethnic groups. Notably, Blacks at greater risk were older and had a positive fluid balance during ventilation, while higher platelets and administration of intermediate dose anticoagulants were protective. Increased risk among white/Hispanic/other race/ethnicity subjects was associated with higher bilirubin at admission and higher maximum lactate.

Similar to other studies, we had a high proportion of elderly subjects admitted to our ICU with a median age at presentation of 68 y (IQR 61–75.5).[5] In this study, however, age was significantly related to death only among Black subjects, who were marginally younger, overall, compared with subjects in the white/Hispanic/other race/ethnic group. Laboratory and clinical findings associated with increased risk of death also differed by race/ethnicity. Among Black subjects, the presence of a higher fluid balance during ventilation and lower platelets at admission were independently associated with risk of death. By contrast, among the other race/ethnic groups, higher bilirubin and higher lactate excursions during hospitalization were identified as marginal risks. Finally, we noted that tocilizumab treatment may have opposite effects in Black and white/Hispanic/other subjects. While this finding needs to be confirmed in other populations as this was a small sample size, it suggests that clinical management may need to consider race when administering tocilizumab.

Interestingly, we found that, in contrast to some prior studies (but not all), most comorbidities were not associated with worse outcomes except for asthma, which was paradoxically associated with increased likelihood of survival, especially in Black subjects.[5,6] Other studies have shown decreased COVID-19 disease severity in individuals with asthma; while the underlying pathophysiology behind this observation is still unclear, some are proposing that the use of inhaled corticosteroids or decreased expression of angiotensin-converting enzyme receptors on epithelial cells may provide partial explanation.[7]

There has been significant controversy regarding prior use of angiotensin-converting enzyme inhibitors and angiotensin receptor blockers as a risk factor for poor outcomes in COVID-19, though most studies have not shown increased risk.[8] Our results confirm that prior treatment with these drugs was not associated with worse outcomes, although a lower percentage of subjects was taking these drugs than expected based on their comorbidities.

We noted that higher procalcitonin and lower fibrinogen levels were associated with worse outcomes as expected, since high procalcitonin levels are associated with worsening disease and bacterial co-infection. A recent meta-analysis showed that an elevated procalcitonin level is associated with ~ 5-fold increased risk of severe COVID-19 (OR 4.76 [95% CI 2.74–8.29]).[9] Furthermore, higher baseline creatinine and increased partial thromboplastin time (but not prothrombin time/international normalized ratio) were also associated with higher likelihood of death. Our results were similar to those reported by Cheng et al,[10] who reported that baseline kidney disease and acute kidney injury were independent risk factors for in-hospital death.

The disease course for COVID-19 has been described by Siddiqui et al[11] in 3 stages. Stage I is the early infection phase, which includes the constitutional symptoms, and it is believed that the viral replication occurs in this phase. Stage II is when most subjects present to the hospital with worsening respiratory symptoms, high fevers, increase ventilation/perfusion, abnormalities on chest radiography or computed tomography, and markedly elevated inflammatory markers such as C-reactive protein, ferritin, and D-dimer. This progresses into stage III, with worsening inflammatory markers and a cytokine storm similar to hemophagocytic lymphohistiocytosis and CAR-T cell cytokine release syndrome. Subjects often end up with multi-organ failure. Most of our subjects likely presented in stage II or III of the disease with markedly elevated inflammatory markers. The inflammatory markers in our subjects were also significantly higher, with median serum ferritin on admission of 988 (IQR 491–2,181), C-reactive protein of 178 (IQR 100–262), and D-dimer of 2,700 (IQR 1,400–5,860). Studies in New York and China have both

shown markedly elevated ferritin, C-reactive protein, erythrocyte sedimentation rate, and D-dimer levels.[5,6,12]

It has been reported that early intubation in subjects with COVID-19 may be associated with improved outcomes. We noted no difference between early and late intubation in our results, although an analysis of the respiratory system mechanics showed results consistent with the traditional management of ARDS. On intubation, the median P_{aO_2}/F_{IO_2} was 63 (IQR 50–105), PEEP was 10 cm H_2O (IQR 7–10), plateau pressure was 25 cm H_2O (IQR 22–30), and compliance was 26 mL/cm H_2O (IQR 21–33). None of these values were significantly different between survivors and in-patient deaths. However, subjects who survived were found to require lower PEEP and F_{IO_2} early after intubation.

These compliance data are lower than what was reported by Gattinoni et al[13] in their initial experience in Italy. Gattinoni et al[13] described 2 phenotypes: phenotype L, with low elastance, low ventilation/perfusion ratio, and low lung recruitability; and phenotype H, with a high elastance, high right-to-left shunt, and high lung recruitability. They recommended that the subjects with phenotype L be managed with a high tidal volume and low PEEP strategy, which is contrary to the ARDSNet protocol. The respiratory mechanics data for subjects with COVID-19 in Boston also support the low compliance ventilation strategy, which remained low over a period of 3 d.[14] The compliance in previous large cohort of studies was also lower, and analysis of our subjects shows similar results.[15,16] In our study on intubation, the median P_{aO_2}/F_{IO_2} was 63 (IQR 50–105) and median compliance was 26 mL/cm H_2O (IQR 21–33), and compliance remained low over the 72 h following intubation.

Interestingly, even though prone positioning has been reported to improve outcomes and was performed on 35% of subjects (of whom 40% survived) in our cohort, it was not associated with increased likelihood of survival.[17] Although prone positioning did point toward better survival (ie, 40% vs 32%, $P = .37$) our sample size was under-powered for it to be statistically significant.

Lastly, data regarding the use of repurposed drugs for the treatment of COVID-19 have been conflicting. Our center attempted several of these therapies in line with the available information at the time. Our post hoc analysis of these interventions demonstrated that only steroid therapy was associated with improved outcomes. The surviving sepsis guidelines recommend the short-term use of steroids for intubated subjects with COVID-19 and ARDS.[18] Wu et al[19] reported reduced risk of death in COVID-19–associated ARDS for subjects who received steroids (hazard ratio 0.38 [95% CI 0.20–0.72], $P = .03$). There was also a trend toward improved outcomes in the group with intermediate-dose anticoagulation, which may merit further attention in light of increased rates of thrombosis associated with COVID-19. Treatment with systemic anticoagulation seemed to have better survival outcomes in a large observational study of subjects with COVID-19 in New York, and a subgroup analysis of mechanically ventilated critically ill subjects indicated similar benefits.[20] However, treatment should be based on a risk/benefit analysis due to risk of bleeding associated with anticoagulation.

Some limitations of this study should be considered when interpreting results. This was a retrospective study in a single center, potentially limiting generalizability. As a descriptive study, it can only show an association with a finding and does not prove cause and effect, and other known and unknown confounders can skew results. Furthermore, given the rapidly changing pace of knowledge regarding treatment of this disease, medical treatments given were layered on each other and introduced at different times, making assessment of the association of in-patient death with any single treatment imprecise. Small sample sizes and missing data for some analyses also reduced the power to detect differences.

Conclusions

Despite similar in-patient mortality from COVID-19, Black subjects and subjects of white/Hispanic/other race or ethnicity appear to have different risk factors and responses to treatments in relation to in-patient death. Increased age, positive fluid balance during ventilation, and low platelet count at admission were independent risk factors for Black subjects, while elevated total bilirubin and elevated maximum lactate are risk factors for other race/ethnic groups. To our knowledge, this is the only paper describing clinical characteristics, respiratory mechanics, and outcomes by race/ethnicity in a predominantly Black population.

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