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Should COVID-19 patients >75 years be Ventilated? An Outcome Study

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Summary

Background: Elderly patients with COVID-19 disease are at increased risk for adverse outcomes. Current data regarding disease characteristics and outcomes in this population are limited.
Aim: To delineate the adverse factors associated with outcomes of COVID-19 patients ≥75 years of age.
Design: Retrospective cohort study.
Methods: Patients were classified into mild/moderate, severe/very severe and critical disease (intubated) based on oxygen requirements. The primary outcome was in-hospital mortality.
Results: A total of 355 patients aged ≥75 years hospitalized with COVID-19 between 19 March and 25 April 2020 were included.Mean age was 84.3 years. One-third of the patients developed critical disease. Mean length of stay was 7.10 days. Vasopressors were required in 27%, with the highest frequency in the critical disease group (74.1%). Overall mortality was 57.2%, with a significant difference between severity groups (mild/moderate disease: 17.4%, severe/very severe disease: 71.3%, critical disease: 94.9%, $P < 0.001$).Increased age, dementia, and severe/very severe and critical disease groups were independently associated with increased odds for mortality while diarrhea was associated with decreased odds for mortality (OR: 0.12, 95% CI: 0.02–0.60, $P < 0.05$). None of the cardiovascular comorbidities were significantly associated with mortality.
Conclusion: Age and dementia are associated with increased odds for mortality in patients ≥75 years of age hospitalized with COVID-19. Those who require intubation have the greatest odds for mortality. Diarrhea as a presenting symptom was associated with lower odds for mortality.

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Introduction

As of early January 2021, the coronavirus (SARS-CoV-2) pandemic remains a public health crisis, affecting more than 84 million people globally and 20 million in the United States (US) alone.[1] Presentations range from an asymptomatic course to severe inflammatory reaction resulting in acute respiratory distress syndrome (ARDS) and multi-organ dysfunction.[2]

Older age, obesity and other comorbid conditions are associated with higher rates of COVID-19 mortality.[3,4] The Centers for Disease Control and Prevention (CDC) reports that although individuals older than age 65 comprise 17% of the total US population, they account for 31% of COVID-19 infections, 45% of hospitalizations, 53% of intensive care unit admissions and 80% of deaths.[5] Similarly, a report from the Chinese Center for Disease Control and Prevention evaluating more than 72 000 cases of COVID-19 reported an overall case fatality rate (CFR) of 2.3%. In contrast, the CFR was 8% in 70–79-year olds and 14.8% in those ≥80 years old.[6] A Chinese study of 201 patients found that older age is associated with a greater risk of developing ARDS and of death.[7]

Elderly patients may have one or more pre-existing medical conditions, which places them at increased risk for developing severe forms of COVID-19 and even of dying from the disease. Physiological changes that accompany aging, including altered immune response and multiple age-related comorbidities (e.g. dementia), are associated with poorer outcomes in older patients.[8]

Very few studies have focused on the characteristics and outcomes of COVID-19 infection in the elderly in the United States; hence, data in this regard are limited. This retrospective single-center study aims to delineate the characteristics, risk factors and outcomes among patients aged ≥75 years hospitalized with COVID-19.

Materials and methods

Study setting

A single-center, retrospective, observational analysis was performed at Maimonides Medical Center, a 711-bed tertiary care teaching hospital in the New York City. The Maimonides Medical Center Institutional Review Board approved the study, qualified it as minimal risk research and waived the need for informed consent.

Patient selection

We analyzed the clinical and demographic characteristics and outcomes of patients aged ≥75 years admitted to Maimonides Medical Center with COVID-19 between 19 March and 25 April 2020. The method for diagnosis of SARS-CoV-2 infection was real-time reverse transcription-polymerase chain reaction testing of a nasopharyngeal sample. All patients included in this study presented to our emergency department (ED) with either symptoms suggestive of COVID-19 infection or had a history of exposure to a person with known COVID-19 infection. Those who presented with symptoms and had a positive result as outpatient were re-tested in our ED to confirm COVID-19 infection. Patients who died within one day of being admitted or during their ED stay prior to being admitted were excluded. Patients seen in the ED or outpatient clinics that did not require hospitalization were also excluded.

Definition of disease severity

Disease severity was determined by the amount of oxygen supplementation required throughout the patient's hospital course. Mild disease severity was defined as an oxygen saturation level >95% on room air. Moderate disease severity was defined as requiring oxygen supplementation via nasal cannula at rates of up to 5 l/min to maintain an oxygen saturation level of ≥95%. Severe disease was defined as any patient with SARS-CoV-2 infection requiring oxygen supplementation via face mask at rates up to 10 l/min to maintain an oxygen saturation level of ≥95%. The disease was considered very severe when requiring oxygen supplementation via non-rebreather mask or high-flow nasal cannula to maintain an oxygen saturation level of ≥95%. The disease was deemed critical when intubation and mechanical ventilation were required.

Data collection

Data collected included patient demographics, presenting symptoms, comorbidities, home medications, initial vital signs upon admission, pertinent laboratory results, treatment received for COVID-19, complications and outcomes, including mortality and length of hospital stay (LOS).

Outcomes

The primary outcome was in-hospital mortality, described as death in hospital following the diagnosis of COVID-19. The secondary outcome was LOS.

Statistical analysis

Descriptive statistics of mean and standard deviation were used to describe continuous variables, whereas frequencies and percentages were used to describe categorical variables. Skewed variables were log-transformed. Troponin had values of 0; therefore, 0.01 was added to all values, which were then log-transformed. Analysis of variance compared continuous variables and Pearson's chi-square test compared categorical variables, except when the expected cell size was <5, in which case the Fisher's exact test was performed. Univariate logistic regression was conducted for the outcome variable of mortality. Any variable that was statistically significant in the univariate analysis for mortality was included in the multivariate analysis. Univariate linear regression was conducted for the outcome variable of LOS. Any variable that was statistically significant in the univariate analysis for LOS was included in the multivariate analysis. All Pvalues were two-tailed. The alpha level for significance was set at $P < 0.05$. IBM SPSS Statistics v. 26 (IBM, Armonk, NY) and Stata SE v. 15 (Stata, College Station, TX) were used for statistical analyses.

Results

Baseline characteristics

There were 355 patients included in the study. The mean age was 84.3 years, and almost half were female. Two-thirds were Caucasian and 7.6% were Hispanic. Hypertension (78.6%), diabetes mellitus (33.8%), heart failure (26.2%) and coronary artery disease (26.2%) were the most common comorbidities. There were 15.8% obese. Shortness of breath (58.9%), fever (49.9%), and cough (41.1%) were the most common presenting symptoms. Table 1 shows the baseline characteristics.

Table 1. Baseline characteristics

Variable	M (SD) or frequency (%) Whole sample ($n = 355$)	M (SD) or frequency (%) Mild/ moderate ($n = 144$)	M (SD) or frequency (%) Severe/ very severe ($n = 94$)	M (SD) or frequency (%) Critical ($n = 117$)	*P*-value
Demographics					
Age (years)	84.3 (6.51)	84.2 (6.54)	85.8 (6.69)	83.2 (6.15)	0.02
Female gender	164 (46.2)	69 (47.9)	46 (48.9)	49 (41.9)	0.51
Race	239 (67.3)	99 (68.8)	58 (61.7)	82 (70.1)	0.41
White	45 (12.7)	21 (14.6)	13 (13.8)	11 (9.4)	
Black	41 (11.5)	12 (8.3)	16 (17.0)	13 (11.1)	
Asian	30 (8.5)	12 (8.3)	7 (7.4)	11 (9.4)	
Other					
Ethnicity	323 (91.0)	131 (91.0)	88 (93.6)	104 (88.9)	0.35
Non-Hispanic	27 (7.6)	12 (8.3)	6 (6.4)	9 (7.7)	
Hispanic	5 (1.4)	1 (0.7)	0 (0.0)	4 (3.4)	
Unknown					
Comorbidities					
Obesity	56 (15.8)	16 (14.2)	12 (14.6)	28 (26.4)	0.04
Smoking	94 (26.5)	38 (26.4)	20 (21.3)	36 (31.0)	0.52
Never	6 (1.7)	4 (2.8)	0 (0.0)	2 (1.7)	
Active	30 (8.5)	12 (8.3)	8 (8.5)	10 (8.6)	
Former	225 (63.4)	90 (62.5)	66 (70.2)	69 (59.0)	
Unknown					
Hypertension	279 (78.6)	108 (75.5)	74 (78.7)	97 (82.9)	0.35
Diabetes mellitus	120 (33.8)	49 (34.3)	30 (31.9)	41 (35.0)	0.89
Cerebrovascular accident	37 (10.4)	9 (6.3)	13 (13.8)	15 (12.8)	0.11
Atrial fibrillation	78 (22.0)	25 (17.5)	23 (24.5)	30 (25.6)	0.23
Heart failure	93 (26.2)	35 (26.1)	25 (28.1)	33 (30.6)	0.75
Chronic obstructive pulmonary disease	34 (9.6)	14 (9.8)	11 (11.7)	9 (7.7)	0.61
Asthma	14 (3.9)	4 (2.8)	5 (5.3)	5 (4.3)	0.62
Deep vein thrombosis/pulmonary embolism	17 (4.8)	7 (4.9)	4 (4.3)	6 (5.1)	0.77
Chronic kidney disease	25 (7.0)	9 (6.3)	6 (6.4)	10 (8.5)	0.75
Coronary artery disease	93 (26.2)	41 (28.7)	21 (22.3)	31 (26.5)	0.56
Cancer	316 (89.0)	123 (86.0)	84 (89.4)	109 (93.2)	0.01
No	17 (4.8)	11 (7.7)	6 (6.4)	0 (0.0)	
Active treatment	21 (5.9)	9 (6.3)	4 (4.3)	8 (6.8)	
Past 5 years					
Dementia	88 (24.8)	27 (18.9)	39 (41.5)	22 (18.8)	<0.001
Presenting symptoms					
Fever	177 (49.9)	64 (45.1)	52 (55.3)	61 (52.1)	0.27
Cough	146 (41.1)	57 (40.1)	34 (36.2)	55 (47.4)	0.24
Anosmia	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.9)	0.60
Ageusia	3 (0.8)	1 (0.7)	2 (2.1)	0 (0.0)	0.27
Myalgia	34 (9.6)	15 (10.6)	4 (4.3)	15 (12.8)	0.10
Nausea	16 (4.5)	9 (6.3)	4 (4.3)	3 (2.6)	0.34
Vomiting	14 (3.9)	9 (6.4)	4 (4.3)	1 (0.9)	0.06
Diarrhea	24 (6.8)	10 (7.0)	9 (9.6)	5 (4.3)	0.31
Shortness of breath	209 (58.9)	59 (41.5)	65 (69.1)	85 (72.6)	<0.001
Chest pain	18 (5.1)	8 (5.6)	6 (6.4)	4 (3.4)	0.56
Vital signs					
Systolic blood pressure [mmHg]	129.6 (24.68)	129.9 (22.53)	129.0 (24.62)	129.6 (27.30)	0.96
Diastolic blood pressure [mmHg]	73.7 (19.07)	74.0 (16.82)	74.0 (19.90)	73.0 (21.00)	0.90
Heart rate [per minute]	93.8 (21.68)	91.1 (20.39)	95.4 (19.86)	95.9 (24.27)	0.15
Oxygen saturation	91.7 (8.08)	94.3 (5.47)	89.6 (9.52)	90.3 (8.67)	<0.001
Respiratory rate [per minute]	24.7 (7.19)	21.4 (4.00)	26.3 (7.82)	27.3 (8.14)	<0.001

Note: Mm mean; SD, standard deviation. Sample size for continuous variables less than 355 are: systolic blood pressure ($n = 353$), diastolic blood pressure ($n = 353$), heart rate ($n = 352$), oxygen saturation ($n = 351$) and respiratory rate ($n = 353$). Sample size for categorical variables missing are: obesity ($n = 54$), hypertension ($n = 1$), diabetes mellitus ($n = 1$), cerebrovascular accident ($n = 1$), atrial fibrillation ($n = 1$), heart failure ($n = 24$), chronic obstructive pulmonary disease ($n = 1$), chronic kidney disease ($n = 2$), asthma ($n = 1$), deep vein thrombosis/pulmonary embolism ($n = 2$), coronary artery disease ($n = 1$), cancer ($n = 1$), dementia ($n = 1$), fever ($n = 2$), cough ($n = 3$), anosmia ($n = 3$), ageusia ($n = 2$), myalgia ($n = 3$), nausea ($n = 2$), vomiting ($n = 3$), diarrhea ($n = 2$), shortness of breath ($n = 2$) and chest pain ($n = 2$).

Table 2. Management and outcomes

Variable	M (SD) or frequency (%) Whole sample ($n = 355$)	M (SD) or frequency (%) Mild/moderate ($n = 144$)	M (SD) or frequency (%) Severe/very severe ($n = 94$)	M (SD) or frequency (%) Critical ($n = 117$)	*P*-value
Laboratory values					
White blood cell,k/μl	9.4 (5.81)	8.6 (5.24)	10.0 (9.67)	9.7 (5.39)	0.01
Lymphocyte count,k/μl	12.5 (9.96)	13.8 (10.82)	11.5 (9.84)	11.9 (8.84)	0.17
Platelets,k/μl	208.5 (95.49)	216.7 (97.85)	214.4 (101.93)	194.2 (86.28)	0.10
Hemoglobin, g/dl	12.3 (2.21)	12.1 (2.21)	12.1 (2.30)	12.5 (2.12)	0.23
Serum sodium, mmol/l	139.3 (8.87)	137.7 (7.49)	142.6 (10.00)	138.7 (8.80)	<0.001
Creatinine, mg/dl	1.83 (1.78)	1.6 (1.38)	1.9 (1.70)	2.1 (2.18)	0.02
C-reactive protein, mg/dl (highest)	18.5 (10.88)	13.2 (8.71)	20.7 (10.87)	22.4 (10.81)	<0.001
Ferritin, ng/ml (highest)	1107.9 (1369.00)	863.3 (1026.64)	944.5 (1126.15)	1478.8 (1724.85)	0.01
D-dimer, ng/ml (highest)	5810.0 (10 920.07)	3257.2 (7377.53)	7812.1 (14 399.90)	6933.7 (10 855.24)	0.02
Lactate dehydrogenase, IU/l (highest)	561.8(546.16)	403.9(166.42)	501.6(240.44)	762.9(825.58)	<0.001
Glomerular filtration rate	44.2 (17.78)	47.6 (16.44)	41.5 (17.94)	42.3 (18.63)	0.02
Troponin ng/ml (highest)	1.0 (5.82)	0.3 (1.62)	1.0 (6.35)	1.6 (7.99)	<0.001
Procalcitonin, ng/ml (highest) [mean]	3.2 (6.90)	2.7 (7.61)	2.0 (2.50)	4.7 (8.10)	0.002
Alanine transaminase, IU/l [mean]	38.6 (63.12)	30.4 (35.16)	36.9 (53.06)	49.9 (89.91)	0.15
Aspartate transaminase, IU/l	69.5 (111.85)	52.6 (54.04)	66.1 (69.88)	92.3 (171.89)	0.001
Intubation	117 (33.0)	0 (0.0)	0 (0.0)	117 (100.0)	—
Treatment management					
Vasopressor	96 (27.0)	4 (2.9)	6 (6.4)	86 (74.1)	<0.001
Hemodialysis	36 (10.1)	6 (4.3)	5 (5.4)	25 (21.4)	<0.001
ECMO support	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.9)	0.61
Blood transfusion	35 (9.9)	7 (5.1)	4 (4.3)	24 (20.5)	<0.001
Hydroxychloroquine	248 (69.9)	76 (54.3)	68 (72.3)	104 (88.9)	<0.001
Azithromycin	258 (72.7)	82 (59.0)	73 (77.7)	103 (88.0)	<0.001
Ritonavir/lopinavir	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.9)	0.60
Steroids	60 (16.9)	8 (5.8)	10 (10.6)	42 (36.2)	<0.001
Prophylactic anticoagulation	232 (65.4)	84 (60.4)	64 (68.8)	84 (73.0)	0.09
Therapeutic anticoagulation	90 (25.4)	28 (20.1)	25 (26.9)	37 (31.6)	0.11
Convalescent plasma	7 (2.0)	1 (0.7)	1 (1.1)	5 (4.3)	0.14
Remdesivir	7 (2.0)	0 (0.0)	0 (0.0)	7 (6.0)	<0.001
Vitamin C	350 (98.6)	42 (30.2)	36 (38.3)	53 (45.3)	0.045
Zinc	105 (29.6)	37 (26.6)	25 (26.6)	43 (36.8)	0.15
Tocilizumab	11 (3.1)	0 (0.0)	2 (2.1)	9 (7.7)	0.001
Antibiotics for suspected bacterial infection	270 (76.1)	82 (59.0)	78 (83.0)	110 (94.0)	<0.001
Complications					
Deep vein thrombosis/ pulmonary embolism	2 (0.6)	1 (0.8)	1 (0.5)	0 (0.7)	0.73
Cerebrovascular accident	3 (0.8)	1 (1.2)	1 (0.8)	1 (1.0)	1.00
Bacteremia/fungemia	36 (10.1)	5 (3.6)	8 (8.6)	23 (19.8)	<0.001
Outcomes					
Mortality	203 (57.2)	25 (17.4)	67 (71.3)	111 (94.9)	<0.001
Length of stay (days)	7.8 (7.10)	5.6 (4.77)	7.7 (5.92)	10.6 (9.14)	<0.001

Note: M, mean; SD, standard deviation. Sample size for continuous variables less than 355 are: white blood cell ($n = 351$), lymphocyte ($n = 317$), platelet ($n = 345$), hemoglobin ($n = 347$), serum sodium ($n = 350$),creatinine ($n = 347$), ferritin ($n = 287$), D-dimer ($n = 156$), lactate dehydrogenase ($n = 298$), glomerular filtration rate—admission ($n = 346$), troponin ($n = 325$), procalcitonin ($n = 270$), alanine transaminase—admission ($n = 313$) and aspartate transaminase—admission ($n = 313$). Sample size for categorical variables missing are: vasopressor ($n = 6$), hemodialysis ($n = 6$), ECMO support ($n = 6$), blood transfusion ($n = 6$), hydroxychloroquine ($n = 4$), azithromycin ($n = 5$), ritonavir/lopinavir ($n = 6$), steroids ($n = 6$), prophylactic anticoagulation ($n = 8$), therapeutic anticoagulation ($n = 6$), convalescent plasma ($n = 5$), remdesivir ($n = 5$), vitamin C ($n = 5$), zinc ($n = 5$), antibiotics for suspected bacterial infection ($n = 5$), diagnosis of deep vein thrombosis/pulmonary embolism ($n = 2$), diagnosis of cerebrovascular accident ($n = 7$) and diagnosis of bacteremia/fungemia ($n = 9$). Comparison between groups reports percentages only for cases analyzed and does not include missing cases. Prophylactic anticoagulation included lovenox 40 mg ($n = 34$, 9.6%),lovenox 60 mg ($n = 73$, 20.6%), heparin ($n = 71$, 20.0%) and low dose apixaban ($n = 54$, 15.2%). Therapeutic anticoagulation included lovenox ($n = 46$, 13.0%), heparin drip ($n = 6$, 1.7%), DOAC ($n = 35$, 9.9%) and coumadin ($n = 3$, 0.8%). Laboratory values are on admission unless otherwise specified.

Table 3. Dementia analysis

Variable	No dementia M (SD) or frequency (%) ($n = 266$)	Yes dementia M (SD) or frequency (%) ($n = 88$)	*P*-value	Dementia mortality Multivariate OR (95% CI) ($n = 88$)	Dementia LOS Multivariate B (SE) ($n = 88$)
Demographics					
Age (years)	83.1 (6.26)	87.9 (5.96)	<0.001	1.03 (0.94, 1.13)	<0.001 (0.01)
Female gender	117 (44.0)	47 (53.4)	0.12	—	—
Comorbidities					
Obesity	45 (20.1)	11 (14.3)	0.26	—	—
Hypertension	211 (79.3)	68 (77.3)	0.68	—	—
Diabetes mellitus	100 (37.6)	20 (22.7)	0.01	2.68 (0.68, 10.58)	−0.04 (0.09)
Heart failure	72 (28.9)	21 (25.6)	0.56	—	—
Disease severity					
Care-group	116 (43.6)	27 (30.7)	<0.001	1.00	Reference
Mild/moderate	55 (20.7)	39 (44.3)		9.81 (2.93, 32.80)**	0.05 (0.09)
Severe/very severe	95 (35.7)	22 (25.0)		53.71 (5.87, 491.38)**	0.24 (0.10)*
Critical					
Complications					
Deep vein thrombosis/ pulmonary embolism	1 (0.4)	1 (1.2)	0.44	—	—
Cerebrovascular accident	1 (0.4)	2 (2.3)	0.16	—	—
Bacteremia/fungemia	25 (9.6)	11 (12.8)	0.40	—	—
Outcomes					
Mortality	140 (52.6)	62 (70.5)	0.003		
LOS (days)	7.9 (7.49)	7.6 (5.83)	0.58		

Note: LOS, length of stay; M, mean; SD, standard deviation; OR, odds ratio; CI, confidence interval; B, unstandardized beta; SE, standard error.
*$P < 0.05$, **$P < 0.001$.

Management

Table 2 shows management and outcome variables. There were 33% that were intubated and 27% required vasopressors, with the highest frequency for vasopressors in the critical disease severity group (74%). There were 10.1% that received hemodialysis and 9.9% received blood transfusions. More than two-thirds received hydroxychloroquine (69.9%) and/or azithromycin (72.7%). Prophylactic antibiotics were administered to 76.1%.

Complications

There were 10.1% diagnosed with bacteremia/fungemia, while <1% had either a cerebrovascular accident or deep venous thrombosis. No statistical difference was found in the occurrence of deep vein thrombosis/pulmonary embolism or cerebrovascular accident based on disease severity. Bacteremia/fungemia were seen more often in patients with critical disease severity (19.8%).

Mortality and LOS

The overall mortality rate was 57.2%, with a significant difference between severity groups. Patients with mild/moderate disease had mortality of 17.4%, those with severe/very severe disease had mortality of 71.3% and those with critical disease had the highest mortality of 94.9% ($P < 0.001$). The mean LOS was 7.10 days. This varied from 4.77 days in patients with mild/moderate disease, 5.92 days for those with severe/very severe disease, to 9.1 days for those with critical disease ($P < 0.001$).

Dementia and disease outcomes

Table 3 shows comparisons between patients with and without dementia. Those with dementia were older, had less diabetes, more severe/very severe disease and less critical disease (i.e. intubated). Those with dementia had a greater percentage for mortality than those without dementia ($P = 0.003$). There was no difference for LOS between those with and without dementia. Both severe/very severe disease ($P < 0.001$) and critical disease ($P < 0.001$) were each significantly associated with increased odds for mortality. Critical disease was significantly associated with increased LOS.

Predictors of LOS

Table 4 shows linear regression analyses for LOS. In the multivariate analysis, female gender, cough, severe/very severe disease, hemodialysis, blood transfusion, steroid use, prophylactic anticoagulation, therapeutic anticoagulation, vitamin C, tocilizumab and antibiotics for suspected bacterial infection were each significantly associated with increased LOS. None of the comorbidities, vital signs, laboratory values and complication variables were significantly associated with LOS.

Predictors of mortality

Table 5 shows logistic regression analyses for mortality. In the multivariate analysis, increased age, dementia, severe/very severe and critical disease were each significantly associated with increased odds for mortality. Conversely, diarrhea was significantly associated with decreased odds for mortality. None of the vital signs, laboratory values, treatment management and complication variables were significantly associated with mortality.

Discussion

The current COVID-19 pandemic has affected the older population most severely. To our knowledge, this study represents the largest US analysis focusing on elderly patients hospitalized

Table 4. Linear regression for hospital length of stay

Variable	Univariate B (SE)	Multivariate B (SE)	Multivariateno mortality B (SE)	Multivariateyes mortality B (SE)
Demographics				
Age (years)	−0.01 (0.003)*	−0.002 (0.003)	—	—
Female gender	0.08 (0.04)#	0.08 (0.04)*	0.16 (0.06)**	0.03 (0.05)
Presenting symptoms				
Cough	0.09 (0.04)*	0.08 (0.04)*	0.02 (0.06)	0.08 (0.05)
Shortness of breath	0.12 (0.04)**	−0.06 (0.04)	—	—
Laboratory values				
C-reactive protein, mg/dl	0.01 (0.002)**	—	—	—
Ferritin, ng/ml (highest)	0.12 (0.05)*	—	—	—
Disease severity				
Mild/moderate	Reference	Reference	Reference	Reference
Severe/very severe	0.17 (0.05)**	0.11 (0.05)*	0.27 (0.07)***	0.05 (0.08)
Critical	0.27 (0.05)***	0.10 (0.06)	0.13 (0.19)	0.07 (0.08)
Treatment management				
Vasopressor	0.22 (0.05)**	−0.12 (0.06)	—	—
Hemodialysis	0.27 (0.07)***	0.15 (0.07)*	0.02 (0.16)	0.14 (0.07)*
Blood transfusion	0.41 (0.07)***	0.24 (0.07)***	0.33 (0.13)*	0.26 (0.07)***
Hydroxychloroquine	0.22 (0.05)***	0.08 (0.06)	—	—
Azithromycin	0.19 (0.05)***		—	—
Steroids	0.33 (0.05)***	0.18 (0.05)**	0.13 (0.12)	0.17 (0.06)**
Prophylactic anticoagulation	0.14 (0.04)**	0.18 (0.05)***	0.26 (0.07)***	0.18 (0.06)**
Therapeutic anticoagulation	0.17 (0.05)***	0.23 (0.05)***	0.33 (0.09)***	0.18 (0.06)**
Convalescent plasma	0.33 (0.15)*	−0.18 (0.14)	—	—
Remdesivir	0.47 (0.15)**	0.12 (0.13)	—	—
Vitamin C	0.28 (0.04)***	0.12 (0.05)*	0.16 (0.06)*	0.15 (0.05)**
Zinc	0.27 (0.04)***	0.09 (0.05)	—	—
Tocilizumab	0.43 (0.12)***	0.25 (0.11)*	0.41 (0.34)	0.19 (0.11)
Antibiotics for suspected bacterial infection	0.31 (0.05)***	0.12 (0.05)*	0.13 (0.06)*	0.08 (0.07)
Complications				
Bacteremia/fungemia	0.30 (0.07)***	0.10 (0.06)	—	—

Note: B, unstandardized beta; SE, standard error. Multivariate whole sample analysis included 334 patients due to missing data. Multivariate no mortality subsample included 145 patients. Multivariate mortality subsample included 196 patients. C-reactive protein and Ferritin were not included in the multivariate analysis due to missing data. For brevity purposes, many variables not statistically significant in the univariate analyses are not shown in the table.Multivariate whole sample adjusted Rsquare = 0.38. Multivariate no mortality subsample adjusted Rsquare = 0.40. Multivariate mortality subsample adjusted R square = 0.33.

#$P = 0.05$, *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$.

Laboratory values are on admission unless otherwise specified.

with COVID-19. Our findings indicate that even in very elderly patients older age is associated with increased mortality. This corroborates previous studies suggesting that advancing age is a risk factor for increased mortality in COVID-19 infection.[9–12]

The overall mortality in our cohort was 57.2%. This number varied significantly among disease severity levels. Hence, patients in the mild to moderate disease group had a mortality of 17.4% while those in the critical disease group had a mortality of 94.9%. Other studies report COVID-19 mortality rates for older patients ranging from 20% to 97%.[9,11,13] This broad variation in mortality rates depends significantly on admission criteria, disease severity and age cutoffs of the patients included in the individual studies. As our study included only inpatients, we anticipated higher mortality rates than other studies that included outpatients or patients seen in the ED and discharged. Intubated patients (critical disease group) in our study had the highest mortality rate. This was similar to the 97% mortality rate found in the subgroup of older COVID-19 patients who required intubation in another study.[13] The high mortality rate in intubated elderly patients in our study and others is likely due to the severity of the disease process that leads to multiorgan failure rather than intubation itself and its complications. Hence, the decision to intubate in this elderly population should be individualized based on the overall clinical picture as would be done in non-COVID patients.

Cardiovascular comorbidities are associated with worse outcomes in COVID-19 patients.[9,14–18] As expected from a study focused on older patients, a higher percentage of hypertension, atrial fibrillation, coronary artery disease, heart failure and cerebrovascular disease were found in our study as compared to reports that included younger patients.[13,19] However, we did not find any association between these comorbidities and mortality.

COVID-19 patients with dementia had a higher mortality rate than those patients without dementia. This contrasts with a study on elderly patients hospitalized with COVID-19 that included 44% of patients with dementia. Although there was a numerically higher mortality in patients with dementia (27% vs. 20%), this was not statistically significant.[20] In a report from Italy of 627 COVID-19 patients admitted to a geriatric service, patients with dementia had a mortality rate of 62% as compared to 26% in those without the disease.[21] However, there was a difference in age between the groups of 13.7 years which was

Table 5. Logistic regression for mortality among elderly COVID-19 patients

Variable	Univariate OR (95% CI)	Multivariate OR (95% CI)
Demographics		
Age (years)	1.05 (1.02, 1.09)**	1.10 (1.02, 1.18)*
Comorbidities		
Hypertension	1.83 (1.09, 3.05)*	1.83 (0.74, 4.56)
Cerebrovascular accident	2.56 (1.17, 5.59)*	1.13 (0.31, 4.15)
Heart failure	1.75 (1.06, 2.88)*	2.36 (0.97, 5.74)
Dementia	2.15 (1.28, 3.60)**	3.02 (1.19, 7.63)*
Presenting symptoms		
Diarrhea	0.28 (0.11, 0.70)**	0.12 (0.02, 0.60)*
Shortness of breath	3.12 (2.01, 4.86)***	1.77 (0.76, 4.12)
Vital signs		
Oxygen saturation	0.94 (0.91, 0.97)***	0.97 (0.92. 1.01)
Respiratory rate [per minute]	772.43 (73.79, 8,085.45)***	1.02 (0.96, 1.09)
Laboratory values		
White blood cell,k/μl	3.30 (1.29, 8.44)*	3.44 (0.64, 18.54)
Serum sodium, mmol/l	1.03 (1.002, 1.05)*	0.96 (0.91, 1.01)
C-reactive protein, mg/dl (highest)	1.08 (1.05, 1.11)***	—
Ferritin, ng/ml (highest)	1.75 (1.04, 2.93)*	—
D-dimer, ng/ml (highest)	2.36 (1.37, 4.08)**	—
Lactate dehydrogenase, IU/l (highest)	36.60 (9.79, 136.92)***	—
Glomerular filtration rate (admission)	0.98 (0.97, 0.996)*	1.00 (0.97, 1.03)
Troponin, ng/ml (highest)	3.17 (2.00, 5.02)***	1.46 (0.63, 3.38)
Aspartate transaminase, IU/l	1.005 (1.001, 1.01)*	—
Disease severity		
Care-group	1.00	1.00
Mild/moderate	11.81 (6.35, 21.98)***	11.00 (4.12, 29.36)***
Severe/very severe	88.06 (34.82, 222.70)***	54.25 (11.84, 248.44)***
Critical		
Treatment management		
Vasopressor	24.44 (9.60, 62.19)***	5.10 (0.82, 31.54)
Hemodialysis	3.49 (1.48, 8.19)**	5.78 (0.85, 39.16)
Blood transfusion	2.32 (1.06, 5.12)*	0.60 (0.11, 3.14)
Hydroxychloroquine	4.26 (2.61, 6.95)***	1.85 (0.61, 5.60)
Azithromycin	3.50 (2.12, 5.77)***	1.33 (0.42, 4.26)
Steroids	4.07 (2.04, 8.15)***	0.62 (0.17, 2.30)
Prophylactic anticoagulation	1.75 (1.12, 2.75)*	1.58 (0.64, 3.91)
Therapeutic anticoagulation	1.62 (0.98, 2.66)	—
Vitamin C	1.59 (1.02, 2.48)*	1.07 (0.45, 2.58)
Antibiotics for suspected bacterial infection	3.26 (1.93, 5.49)***	0.55 (0.20, 1.50)
Complications		
Bacteremia/fungemia	3.46 (1.47, 8.13)**	0.72 (0.17, 3.08)

Note: OR, odds ratio; CI, confidence interval. Multivariate analysis included 289 patients due to missing data. C-reactive protein, ferritin, D-dimer, lactate dehydrogenase and aspartate transaminase at admission were not included in the multivariate analysis due to missing data. For brevity purposes, many variables not statistically significant in the univariate analyses are not shown in the table.

*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$.

Laboratory values are on admission unless otherwise specified.

statistically significant and could have accounted for the difference in mortality. Interestingly, even though our study showed dementia to be associated with higher mortality, less patients with this condition were in the critical disease severity group. This could be explained by a higher proportion of demented patients undergoing palliative care and their families declining aggressive interventions, including intubation.

The obesity rate in our study was significantly lower compared to the general population. Although obese patients were more likely to be in the critical disease group, obesity was not included in the mortality analysis due to missing data on BMI in 56 patients. A recent study in general population found that obesity was associated with higher mortality.[10]

Studies report the incidence rate of diarrhea in COVID-19 patients to range from 2% to 50%.[22–24] We found diarrhea as a presenting symptom in 6.8% of patients, and its presence was associated with decreased mortality. In a previous study by our group, diarrhea was associated with lower mortality in COVID-19 patients with high oxygen requirements.[25] In contrast, another report found COVID-19 patients with diarrhea, nausea and vomiting to be more likely to develop ARDS requiring mechanical ventilation as compared to patients without gastrointestinal symptoms.[26]

Our study has some limitations. First, we did not collect data on certain atypical symptoms, such as delirium and altered mental status, which may be particularly relevant in the older

population. Second, we have no follow-up data on discharged patients to determine post-discharge mortality and readmission rates. However, our focus was to characterize hospitalized patients and determine their outcomes. Third, we did not include information regarding goals of care, which is of paramount importance in the very elderly, especially with a disease process as lethal as COVID-19. Although our study is one of the largest analyses to date focusing on the very elderly, further research is needed in this population to address these topics.

Conclusion

Age and dementia are important risk factors for mortality in patients ≥75 years of age hospitalized with COVID-19. Patients who require intubation have the greatest odds for dying. Patients who reported diarrhea as a presenting symptom had lower mortality than those who did not. Furthermore, although cardiovascular comorbidities are more frequent in the older population, these comorbidities were not associated with mortality in our study.

Conflict of interest. None declared.

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