Predictors of Death, Survival, Need for Intubation, and Need for Oxygen Support Among Admitted COVID-19 Patients of the Veterans Affairs Greater Los Angeles Healthcare System

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ABSTRACT

Introduction:
While risk factors for severe COVID-19 infections have been well explored among the public, population-specific studies for the U.S. Veteran community are limited in the literature. By performing a comprehensive analysis of the demographics, comorbidities, and symptomatology of a population of COVID-19 positive Veterans Affairs (VA) patients, we aim to uncover predictors of death, survival, need for intubation, and need for nasal cannula oxygen support among this understudied community.

Materials and Methods:
A retrospective review was conducted of 124 COVID-19 Veteran patients who were admitted from March to October 2020 to the VA Greater Los Angeles Healthcare System (IRB#2020-000272). Chi-square and Fisher's exact tests were employed to assess differences in baseline demographic and clinical variables between Veterans who survived COVID-19 versus those who succumbed to COVID-19 illness. Multivariate logistic regression and Cox regression analyses were employed to assess predictors of outcome variables, including death, survival, need for intubation, and need for oxygen support (via nasal cannula). Covariates included a wide range of demographic, comorbidity-related, symptom-related, and summary index variables.

Results:
Our study population consisted of primarily senior (average age was 73) Caucasian and African American (52.5% and 40.7%, respectively) Veterans. Bivariate analyses indicated that need for intubation was significantly associated with mortality ($P = 0.002$). Multivariate analyses revealed that age ($P < 0.001$, adjusted odds ratio (OR) = 1.16), dyspnea ($P = 0.015$, OR = 7.73), anorexia ($P = 0.022$, OR = 16.55), initial disease severity as classified by WHO ($P = 0.031$, OR = 4.55), and having more than one of the three most common comorbidities (hypertension, diabetes, and cardiac disease) and symptoms (cough, fever, and dyspnea) among our sample ($P = 0.009$; OR = 19.07) were independent predictors of death. Furthermore, age ($P < 0.001$, hazard ratio (HR) = 1.14), cerebrovascular disease ($P = 0.022$, HR = 3.76), dyspnea ($P < 0.001$, HR = 7.71), anorexia ($P < 0.001$, HR = 16.75), and initial disease severity as classified by WHO ($P = 0.025$, HR = 3.30) were independent predictors of poor survival. Finally, dyspnea reliably predicted need for intubation ($P = 0.019$; OR = 29.65).

Conclusions:
Several independent predictors of death, survival, and need for intubation were identified. These risk factors may provide guidelines for risk-stratifying Veterans upon admission to VA hospitals. Additional investigations of COVID-19 prognosis should be conducted on the larger U.S. Veteran population to confirm our findings and add to the current body of literature.

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INTRODUCTION

The Coronavirus Disease (COVID-19), caused by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-Cov-2), has been spreading globally since December 2019.[1] Since then, COVID-19 has caused more than 30 million infections and 600,000 deaths in the USA as of August 2021, rendering it the public health crisis of the recent decade.[2]

To better manage and mitigate the pandemic, studies have searched for risk factors for developing severe illness from

COVID-19. Thus far, age, sex, obesity, and active cancer have been consistently linked to worse overall health outcomes among COVID-19 patients.[3,4] Notably, the incidence rate ratio for death for those who were 65 years or older was found to be more than 62 times higher than that of those under 65 years old, and the mortality rate of males was 77% higher than that of females.[4]

The U.S. Veteran population predominantly consists of individuals of older age and of the male sex, both of which are risk factors for severe COVID-19 as mentioned above. Additionally, patients treated at Veterans Affairs (VA) hospitals were shown to possess disadvantaged socioeconomic status and chronic psychiatric and medical conditions at higher rates compared to their civilian counterparts.[5] Yet, a recent study discovered that despite being more likely to have risk factors of severe COVID-19 infections, Veterans exhibited lower excess COVID-19 mortality rate compared to the general population.[6] Therefore, while risk factors of severe COVID-19 infections have been extensively studied among the general population,[3,4] it remains unclear whether the same risk factors are applicable to this population. Thus, this unique community merits special attention in the literature.

However, population-specific COVID-19 analyses for VA patients remain limited. Most studies have focused on general trends in population disease severity, racial disparities in testing and hospitalization, and predictors of hospitalization.[7–13] While several studies have investigated risk factors for severe COVID-19 among Veterans, multivariate survival analysis has not been conducted to explore factors contributing to shorter survival length.[14–20]

In this study, we present the clinical outcomes of a cohort of Veteran patients who were admitted to the Greater Los Angeles VA hospitals for COVID-19. We conduct a comprehensive analysis of the demographics, comorbidity profile, interventions, and clinical manifestations of this group of Veterans to investigate independent predictors of death, survival, need for intubation, and need for oxygen support that may inform clinical management in future care for VA patients.

METHODS

Data Collection and Study Population

We conducted a retrospective review of COVID-19 patients who were admitted to the Veterans Affairs Greater Los Angeles Healthcare System (VAGLAHS) from March to October 2020. Among the three campuses that serve 1.4 million Veterans, we identified 135 COVID-19 cases. Survived patients with less than 30 days of follow-up data since diagnosis of COVID-19 were excluded. According to which, 11 cases were excluded, leaving 124 cases for analysis. Data were pooled from the VA electronic medical record system. Study approval was obtained from the VAGLAHS Institutional Review Board (IRB#2020-000272).

Variables of Interest

The outcome variables included mortality, survival, need for intubation, and need for oxygen support (via nasal cannula). Mortality, need for intubation, and need for oxygen support were dichotomous variables determined by clinical records. Survival was determined by the length of survival (days) since date of COVID-19 diagnosis. Several dates were retrieved from Veterans' medical records to calculate this length: date of COVID-19 diagnosis, date of death, and date of last follow-up. If a participant passed away during the follow-up period, this length was determined by the number of days from diagnosis to death.

Covariates of interest included demographic information such as age, sex, race, and ethnicity; comorbidities such as hypertension, diabetes, cardiac disease, cerebrovascular disease, chronic kidney disease, chronic lung disease, and history of cancer (including malignant solid tumor and hematological malignancies); clinical presenting symptoms such as cough, fever, dyspnea, anorexia, tachycardia, malaise, diarrhea, tachypnea, fatigue, chest tightness/pain, nausea/vomiting, abdominal pain, runny nose, and sore throat. All covariates were treated as dichotomous variables except age and race. Age was treated as a continuous variable and race was treated as a nominal variable. Categorization of race and ethnicity are indicated in Table I. These variables are included in this study to characterize the demographic profile of our sample. Options were defined by VAGLAHS's electronic medical records.

We also recorded severity of initial disease presentation to a medical center based on World Health Organization (WHO) guidelines: mild, moderate, and severe.[21] This variable was converted into a dichotomous variable with two levels: "mild" and "moderate to severe". Furthermore, each patient's body mass index (BMI) value was classified into one of the obesity categories according to WHO cutoffs: $<18.5\,\text{kg/m}^2$ (underweight), 18.5–$24.9\,\text{kg/m}^2$ (normal), 25–$29.9\,\text{kg/m}^2$ (overweight), and $\geq 30\,\text{kg/m}^2$ (obese).[22] No participant had a BMI in the underweight range.

Finally, we calculated six dichotomous summary index variables that were felt to be useful clinically: "Having 2+ top 3 comorbidities," "Having 2+ top 3 symptoms," "Having 2+ top 3 comorbidities and symptoms," Having 2+ comorbidities", "Having 2+ symptoms," and "Having 2+ comorbidities and symptoms." Top 3 comorbidities and symptoms were the most frequently reported comorbidities and symptoms by participants in our sample, which included hypertension, diabetes, and cardiac disease versus cough, fever, and dyspnea, respectively.

Statistical Analyses

Chi-square tests and Fisher's exact tests were employed to examine differences in baseline demographic and intervention variables between deceased and survived participants. Additionally, a multiple logistic regression model was employed

TABLE I. Summary of Participant Demographic, Hospital Intervention, and Comorbidity Variables

	Died	Survived	Overall	
Total Cases	$N = 34$ (100%)	$N = 90$ (100%)	$N = 124$ (100%)	Bivariate tests
Demographic Variables				
Average Age	81.35	70.99	73.64	–[a]
Sex[d]				
Male	34 (100.0%)	85 (95.5%)	119 (96.7%)	
Female	0 (0%)	4 (4.5%)	4 (3.3%)	$P = 0.58$[b]
Race[d]				
Caucasian	17 (53.1%)	45 (52.3%)	62 (52.5%)	
African American	12 (37.5%)	36 (41.9%)	48 (40.7%)	$P = 0.76$[b]
Other	3 (9.4%)	5 (5.8%)	8 (6.8%)	
Ethnicity				
Hispanic or Latino	4 (11.8%)	13 (14.4%)	17 (13.7%)	
Not Hispanic or Latino	30 (88.2%)	77 (85.6%)	107 (86.3%)	$P = 0.93$[b]
Body Mass Index[d]				
Normal	11 (42.3%)	32 (36.8%)	43 (38.1%)	
Overweight	10 (38.5%)	28 (32.2%)	38 (33.6%)	–[a]
Obese	5 (19.2%)	27 (31.0%)	32 (28.3%)	
Interventions				
Nasal Cannula				
Utilization	10 (29.4%)	21 (23.3%)	31 (25.0%)	
No Utilization	24 (70.6%)	69 (76.7%)	93 (75.0%)	$P = 0.49$
Intubation				
Utilization	10 (29.4%)	7 (7.8%)	17 (13.7%)	
No Utilization	24 (70.6%)	83 (92.2%)	107 (86.3%)	$P = 0.002$
Comorbidity				
Hypertension				
Yes	27 (79.4%)	63 (70.0%)	90 (72.6%)	
No	7 (20.6%)	27 (30.0%)	34 (27.4%)	–[a]
Diabetes				
Yes	13 (38.2%)	51 (56.7%)	64 (51.6%)	
No	21 (61.8%)	39 (43.3%)	60 (48.4%)	–[a]
Cardiac Disease				
Yes	18 (52.9%)	43 (47.8%)	61 (49.2%)	
No	16 (47.1%)	47 (52.2%)	63 (50.8%)	–[a]
Cerebrovascular Disease				
Yes	14 (41.2%)	26 (28.3%)	40 (32.3%)	
No	20 (58.8%)	64 (71.1%)	84 (67.7%)	–[a]
Chronic Kidney Disease				
Yes	7 (20.6%)	16 (17.8%)	23 (18.5%)	
No	27 (79.4%)	74 (82.2%)	101 (81.5%)	–[a]
Chronic Lung Disease				
Yes	8 (23.5%)	14 (15.6%)	22 (17.7%)	
No	26 (76.5%)	76 (84.4%)	102 (82.3%)	–[a]
Cancer				
Yes	7 (20.6%)	5 (5.6%)	12 (9.7%)	
No	27 (79.4%)	85 (94.4%)	112 (90.3%)	–[c]

[a]Variable is included in multivariate analysis.
[b]Fisher's exact test was employed instead of chi-square tests for any variable that yielded one or more expected values of less than 5.
[c]Rare event exclusion.
[d]Minor data missing, percentages are calculated among those with available data.

with death as the dichotomous outcome variable and demographic, comorbidity, and clinical manifestation variables as covariates. Variable selections were based on whether there were sufficient case numbers for each cell in crosstab tables. Covariates that resulted in case numbers of five or less in any of the observed counts were excluded from the model, leaving age, hypertension, diabetes, cardiac disease, cerebrovascular disease, chronic kidney disease, chronic lung disease, cough, fever, dyspnea, and anorexia as covariates for the model. Since only five patients who died had a BMI in the obese range, BMI was converted to a dichotomous variable (normal versus overweight or obese) and also included in multivariate models. Initial disease severity and summary index variables were also examined as covariates in a separate

model with the same outcome variable to avoid effects of collinearity.

Additionally, the covariates outlined above were also entered into a Cox regression model with survival as the outcome variable and two logistic regression models with need for intubation and need for nasal cannula as the outcome variables.

Alpha level was set at 0.05. Due to the large number of statistical tests being performed in this study, *P*-value adjustments were performed based on the Benjamini–Hochberg method (False Discovery Rates) to minimize risks of alpha inflation. Adjustments were made within each hypothesis in multivariate models. All statistical analyses were performed using IBM SPSS 27.0.1.0.

RESULTS

A summary of all study variables and bivariate analyses is presented in Tables I and II. The average age of our sample was 74 years old, and most participants were Caucasian males of non-Hispanic or Latino descent. A quarter of participants required nasal cannula oxygen support; 13.7% of participants required intubation; and 27.4% of participants died during the study period. Average length of follow-up for participants who survived throughout their follow-up periods was 210 days (standard deviation, 77 days) and the median length was 234 days (range, 31–298 days).

Hypertension, diabetes, cardiac disease, cerebrovascular disease, and chronic kidney disease were the top 5 most common comorbidities among our sample, respectively. Hypertension (72.6%) and diabetes (51.6%) were reported by more than half of all participants (Table I). Cough, fever, dyspnea, anorexia, and tachycardia were the top 5 most reported symptoms among our sample, respectively. Cough (34.7%), fever (34.7%), and dyspnea (31.5%) were reported by more than a third of all participants (Table II).

Bivariate analysis revealed that need for intubation ($P = 0.002$) was significantly associated with death. All other demographic variables, including sex, race, and ethnicity were not significantly different between survived and deceased patients ($P > 0.05$ for all).

Results from multivariate analyses for death and survival are presented in Table III. Logistic regression analysis revealed that age ($P < 0.001$; adjusted odds ratio (OR) = 1.16), dyspnea ($P = 0.015$; OR = 7.73), and anorexia ($P = 0.022$; OR = 16.55) were independent predictors of death when all other comorbidities and symptoms were controlled for. In the summary index model, age ($P = 0.002$; OR = 1.12), initial disease severity ($P = 0.031$; OR = 4.55), and having two or more of the top 3 comorbidities and symptoms ($P = 0.009$; OR = 19.07) were independent predictors of death. On the other hand, having two or more of top 3 comorbidities was linked to lower risks of death ($P = 0.005$; OR = 0.06).

Cox regression analysis revealed that age ($P < 0.001$; hazard ratio (HR) = 1.14), cerebrovascular disease ($P = 0.022$; HR = 3.76), dyspnea ($P < 0.001$; HR = 7.71), and anorexia ($P < 0.001$; HR = 16.75) were independent predictors of poor survival. In the summary index model, age ($P < 0.001$; HR = 1.10) and initial disease severity ($P = 0.025$; HR = 3.30) were independent predictors of worse survival. Having two or more of top 3 comorbidities was predictive of better survival ($P = 0.005$; HR = 0.16).

Results from multivariate tests for need for intubation and nasal cannula oxygen support are shown in Table IV. Logistic regression analyses revealed that dyspnea ($P = 0.019$; OR = 29.65) was an independent predictor of need for intubation. None of the covariates examined was independently related to need for nasal cannula.

DISCUSSION

Among our sample of COVID-19 patients, most were Caucasian males, above the age of 65 years, and with a history of hypertension or diabetes. Multivariate analyses identified several independent predictors of death and poor survival, including age, cerebrovascular disease, dyspnea, anorexia, initial disease severity, and having two or more of the top 3 comorbidities and symptoms. In addition, a clinical manifestation of dyspnea was independently predictive of intubation use.

Demographic Risk Factors

The broader literature has consistently identified age as a significant predictor of worse overall health outcome for Veterans who contract COVID-19.[13–17,20,23] This finding is also well established in the literature for the general population.[3,24] Our finding similarly suggests that age is not only a robust predictor of death, but also linked to worse overall survival. A potential explanation for this trend is immune senescence, which suggests that the slower response of macrophages upon infections and the reduction in size and number of T-cells in older adults result in more pronounced viral replication and severe disease.[25] As the U.S. Veteran population largely consists of older adults, special attention and intentional preventative efforts against COVID-19 transmission are needed.

Comorbidity-Related Risk Factors

Cerebrovascular diseases have been reliably linked to higher risks of severe COVID-19 and death among the general population.[26,27] Similarly, we found that the hazard rates of participants with cerebrovascular disease were 3.8 times higher than those without, suggesting a significant link between cerebrovascular disease and worse survival. This link may be explained by the multifactorial mechanism in which SARS-Cov-2 increases risks for stroke, a risk that may be even higher among patients with existing cerebrovascular disease. Specifically, physiological response to COVID-19 include hyperinflammatory state, hyper-coagulant state, endothelial dysfunction, or hypoxic microvascular diseases, which can eventually result in ischemic or hemorrhagic stroke.[27]

TABLE II. Summary of Participant Disease Presentation Variables

Total Cases	Death N = 34 (100%)	Survived N = 90 (100%)	Overall N = 124 (100%)	Bivariate tests
Presentation				
Initial Disease Severity[c]				_[a]
Moderate to Severe	19 (57.6%)	19 (22.6%)	38 (32.5%)	
Mild	14 (42.4%)	65 (77.4%)	79 (67.5%)	
Cough				_[a]
Yes	12 (35.3%)	31 (34.4%)	43 (34.7%)	
No	22 (64.7%)	59 (65.6%)	81 (65.3%)	
Fever				_[a]
Yes	12 (35.3%)	31 (34.4%)	43 (34.7%)	
No	22 (64.7%)	59 (65.6%)	81 (65.3%)	
Dyspnea				_[a]
Yes	16 (47.1%)	23 (25.6%)	39 (31.5%)	
No	18 (52.9%)	67 (74.4%)	85 (68.5%)	
Anorexia				_[a]
Yes	6 (17.6%)	7 (7.8%)	13 (10.5%)	
No	28 (82.4%)	83 (92.2%)	111 (89.5%)	
Tachycardic				_[b]
Yes	3 (8.8%)	8 (8.9%)	11 (8.9%)	
No	31 (91.2%)	82 (91.1%)	113 (91.1%)	
Malaise				_[b]
Yes	4 (11.7%)	7 (7.8%)	11 (8.9%)	
No	30 (88.3%)	83 (92.2%)	113 (91.1%)	
Diarrhea				_[b]
Yes	1 (2.9%)	9 (5.6%)	10 (8.1%)	
No	33 (97.1%)	81 (94.4%)	114 (91.9%)	
Tachypnea				_[b]
Yes	4 (11.8%)	5 (5.6%)	9 (7.3%)	
No	30 (88.2%)	85 (94.4%)	115 (92.7%)	
Fatigue				_[b]
Yes	3 (8.8%)	4 (4.4%)	7 (5.6%)	
No	31 (91.2%)	86 (95.6%)	117 (94.4%)	
Chest Tightness/Pain				_[b]
Yes	1 (2.1%)	4 (4.4%)	5 (4.0%)	
No	33 (97.1%)	86 (95.6%)	119 (96.0%)	
Nausea/Vomiting				_[b]
Yes	2 (5.9%)	4 (4.4%)	6 (4.8%)	
No	32 (94.1%)	86 (95.6%)	118 (95.2%)	
Abdominal Pain				_[b]
Yes	2 (5.9%)	2 (2.2%)	4 (3.2%)	
No	32 (94.1%)	88 (97.8%)	120 (96.8%)	
Lightheadedness				_[b]
Yes	2 (5.9%)	3 (3.3%)	5 (4.0%)	
No	32 (94.1%)	87 (96.7%)	119 (96.0%)	
Running Nose				_[b]
Yes	2 (5.9%)	1 (1.1%)	3 (2.4%)	
No	32 (94.1%)	89 (98.9%)	121 (97.6%)	
Sore Throat				_[b]
Yes	1 (2.9%)	1 (1.1%)	2 (1.6%)	
No	33 (97.1%)	89 (98.9%)	122 (98.4%)	

[a]Variable is included in multivariate analysis.

[b]Rare event exclusion.

[c]Minor data missing, percentages are calculated among those with available data.

Although the link between cerebrovascular disease and severe COVID-19 infections is well established among the general population, limited studies on the Veteran population have yielded similar results. Our finding suggests that a background of cerebrovascular disease poses significant risks for Veterans who contract COVID-19. Additional studies on VA patients are needed to confirm our findings that are specific to this population.

While it is well established in the literature that underlying cardiovascular comorbidities are risk factors of

TABLE III. Logistic Regression and Cox Regression Analyses for Death and Survival (Adj. Sig. = adjusted *P*-value after Implementation of the Benjamini–Hochberg Method; Adj. O.R.= Adjusted Odds Ratio; C.I. = Confidence Interval; BMI = Body Mass Index)

	Logistic Regression: Outcome = Death (N = 113)[d]			Cox Regression: Outcome = Survival (N = 113)[c, d]		
	Log Odds	Adj. O.R. (95% C.I.)	Adj. Sig.	Log Odds	Adj. O.R. (95% C.I.)	Adj. Sig.
Age	0.15	1.16 (1.08–1.24)	<0.001*	0.13	1.14 (1.08–1.20)	<0.001*
Overweight or Obese BMI	−0.23	0.79 (0.22–2.91)	0.77	0.08	1.09 (0.43–2.78)	0.91
Hypertension	−0.39	0.68 (0.16–2.91)	0.71	−0.04	0.96 (0.33–2.79)	0.89
Diabetes Mellitus	−0.58	0.56 (0.16–1.95)	0.58	−0.61	0.55 (0.21–1.42)	0.34
Cardiac Disease	−0.95	0.39 (0.11–1.43)	0.27	−1.00	0.37 (0.14–0.98)	0.11
Cerebrovascular Disease	0.99	2.69 (0.77–9.37)	0.23	1.33	3.76 (1.42–9.97)	0.022*
Chronic Kidney Disease	0.52	1.67 (0.40–7.02)	0.65	0.31	1.36 (0.45–4.07)	0.74
Chronic Lung Disease	0.62	1.85 (0.41–8.29)	0.62	0.65	1.91 (0.68–5.33)	0.32
Cough	0.39	1.48 (0.37–5.90)	0.74	0.65	1.92 (0.72–5.11)	0.33
Fever	−0.21	0.81 (0.20–3.24)	0.73	0.09	1.10 (0.41–2.98)	0.95
Dyspnea	2.05	7.73 (1.93–30.92)	0.015*	2.04	7.71 (2.66–22.30)	<0.001*
Anorexia	2.81	16.55 (2.17–125.97)[a]	0.022*	2.82	16.75 (4.16–67.46)	<0.001*
	Logistic Regression: Outcome = Death (N = 117)[b]			Cox Regression: Outcome = Survival (N = 113)[b, c]		
Age	0.11	1.12 (1.05–1.19)	0.002*	0.09	1.10 (1.05–1.14)	<0.001*
Initial Disease Severity	1.51	4.55 (1.40–14.71)	0.031*	1.20	3.30 (1.37–7.98)	0.025*
Having 2+ top 3 comorbidities	−2.84	0.06 (0.01–0.31)	0.005*	−1.85	0.16 (0.05–0.49)	0.005*
Having 2+ top 3 symptoms	−1.81	0.16 (0.02–1.43)	0.24	−0.83	0.44 (0.09–2.11)	0.41
Having 2+ top 3 comorbidities and symptoms	2.95	19.07 (1.60–227.81)[a]	0.009*	1.61	4.98 (0.76–32.45)	0.20
Having 2+ comorbidities	1.99	7.32 (0.63–84.52)	0.23	1.36	3.88 (0.64–23.68)	0.27
Having 2+ symptoms	0.58	1.78 (0.15–21.87)	0.73	0.26	1.30 (0.21–7.90)	0.92
Having 2+ comorbidities and symptoms	−0.46	0.63 (0.03–12.90)	0.77	−0.18	0.84 (0.10–7.36)	0.87

*$P < 0.05$.

[a] Overblown upper bands of 95% confidence intervals are due to rare events and low expected counts in some cells.
[b] Missing initial disease severity data for seven patients.
[c] Missing length of follow-up data for four patients.
[d] Missing BMI data for 11 patients.

TABLE IV. Logistic Regression Analyses for Need for Intubation and Nasal Cannula (Adj. Sig. = adjusted *P*-value after Implementation of the Benjamini–Hochberg Method; Adj. O.R.= Adjusted Odds Ratio; C.I. = confidence Interval; BMI = body Mass Index)

	Logistic Regression: Outcome = Intubation (N = 113)[c]			Logistic Regression: Outcome = Nasal Cannula (N = 113)[c]		
	Log Odds	Adj. O.R. (95% C.I.)	Adj. Sig.	Log Odds	Adj. O.R. (95% C.I.)	Adj. Sig.
Age	0.03	1.03 (0.94–1.12)	0.90	−0.02	0.98 (0.94–1.03)	1.00
Overweight or Obese BMI	0.25	1.29 (0.21–7.82)	0.93	0.29	1.33 (0.46–3.86)	0.94
Hypertension	−3.15	0.04 (0.00–0.42)	0.07	−0.11	0.90 (0.29–2.77)	0.95
Diabetes Mellitus	−0.56	0.57 (0.10–3.45)	0.93	0.33	1.39 (0.51–3.73)	1.00
Cardiac Disease	0.71	2.04 (0.29–14.49)	1.01	−0.13	0.88 (0.30–2.56)	0.97
Cerebrovascular Disease	0.34	1.41 (0.21–9.32)	0.92	0.04	1.04 (0.36–3.00)	0.94
Chronic Kidney Disease	2.12	8.31 (1.11–61.98)	0.15	−2.52	0.08 (0.00–0.70)	0.42
Chronic Lung Disease	1.11	3.04 (0.39–24.03)	0.79	−0.36	0.70 (0.19–2.54)	1.02
Cough	0.41	1.50 (0.28–8.01)	0.93	−0.16	0.86 (0.28–2.61)	1.00
Fever	2.06	7.87 (1.38–44.87)	0.10	0.52	1.69 (0.59–4.79)	1.00
Dyspnea	3.39	29.65 (3.86–228.07)[a]	0.019*	0.43	1.54 (0.53–4.42)	1.00
Anorexia	−0.58	0.56 (0.03–10.87)	0.95	0.78	2.17 (0.45–10.54)	1.00
	Logistic Regression: Outcome = Intubation (N = 117)[b]			Logistic Regression: Outcome = Nasal Cannula (N = 117)[b]		
	Log Odds	Adj. O.R. (95% C.I.)	Adj. Sig.	Log Odds	Adj. O.R. (95% C.I.)	Adj. Sig.
Age	−0.001	1.0 (0.95–1.05)	0.97	−0.01	0.99 (0.95–1.03)	0.94
Initial Disease Severity	1.58	4.87 (1.30–18.30)	0.12	−0.09	0.91 (0.32–2.58)	0.91
Having 2+ top 3 comorbidities	−1.02	0.36 (0.04–3.33)	0.87	−0.03	0.97 (0.26–3.59)	0.91
Having 2+ top 3 symptoms	−0.93	0.39 (0.03–5.17)	0.91	−0.52	0.60 (0.11–3.18)	1.00
Having 2+ top 3 comorbidities and symptoms	2.57	13.00 (0.58–293.02)[a]	0.34	0.46	1.59 (0.20–12.52)	0.90
Having 2+ comorbidities	−0.36	0.70 (0.05–9.99)	0.89	1.35	3.85 (0.34–43.54)	1.32
Having 2+ symptoms	−0.18	0.84 (0.08–9.02)	0.93	1.86	6.41 (0.56–73.27)[a]	1.28
Having 2+ comorbidities and symptoms	0.05	1.05 (0.04–25.34)	0.93	−1.91	0.15 (0.01–2.23)	1.06

*$P < 0.05$.
[a]Overblown upper bands of 95% confidence intervals are due to rare events and low expected counts in some cells.
[b]Missing initial disease severity data for seven patients;.
[c]Missing BMI data for 11 patients.

COVID-19 mortality for both Veterans and civilians,[15,26–28] limited studies have explored cardiac diseases specifically. Unlike cardiovascular disease, cardiac disease refers to pathology associated with specifically the heart, which could encapsulate diseases beyond coronary artery disease, such as valvular issues or congenital defects. In our study, we evaluated cardiac conditions specifically and did not observe a clear link between this comorbidity and health outcomes among COVID-19 Veterans. Cardiac disease should be segregated from cardiovascular diseases and further analyzed in future COVID-19 studies.

Symptomatology Related Risk Factors

Dyspnea was previously shown to be significantly associated with higher risks of mortality and requiring intubation in both the general and Veteran populations.[14,29] Similarly, we found that Veteran patients who reported dyspnea as a clinical manifestation had 7.7 times higher risks of mortality and 7.7 times higher odds of poor survival compared do those who did not. Further, we also found that dyspneic patients were 30 times more likely to require intubation, which is significantly associated with mortality. During the study period, intubation was thought of as one of the best treatment options for patients with hypoxia. Of note the emergence of new strategies,

proning and better therapeutic regimens have reduced the overall need for intubation since the time period of this review.[30,31] Nevertheless, the above evidence suggests that early signs of dyspnea among Veterans may signify a likely moderate to severe disease course and poor health outcomes.

In addition, we found that anorexia was independently linked to a 17-fold increase in both hazard rates and mortality risks. Although anorexia has not been commonly linked to severe COVID-19 in the past, our finding suggests that loss of appetite could be a serious indicator of mortality among Veteran COVID-19 patients.[32] This link can be potentially explained by the poor nutritional and immune status of patients experiencing anorexia, which results in their inability to thwart severe viral infections. This is one of the first studies to identify anorexia as a risk factor for mortality due to COVID-19. Additional attention in the literature regarding anorexia among COVID-19 patients is warranted.

Clinical Summary Index Risk Factors

Initial disease severity based on WHO guidelines[21] was found to be independently predictive of death and worse survival. Particularly, compared to Veterans with mild initial disease, those with moderate to severe initial diseases were 4.6 times more susceptible to mortality and 3.3 times more likely

to have poor survival. Therefore, our finding suggests that WHO's guidelines on initial disease severity may be helpful in risk-stratifying VA patients upon admission for COVID-19. The Care Assessment Need (CAN) score, an existing risk assessment index employed by other VA hospitals, has also been found to reliably predict hospital admission, prolonged stay, mechanical ventilation use, and death.[33] It may be beneficial, then, to evaluate patients who report to VA hospitals for COVID-19 with both WHO's guidelines for initial disease severity and CAN scores.

Our analysis revealed that while having multiple top comorbidities improved participants' survival, having multiple top symptoms in addition to having multiple top comorbidities increased risks of death by a factor of 19. This suggests that comorbidity profile alone is insufficient in determining risks of mortality and severity may also play a role. Response to COVID-19 for patients with chronic conditions can be largely heterogeneous; some patients may not suffer severely from COVID-19 despite a background of multiple chronic diseases.[34] On the other hand, exhibiting multiple top symptoms in addition to having multiple top comorbidities more clearly points to a severe COVID-19 infection exacerbated by chronic conditions. Consequently, this index reliably predicted death in our study. Our finding suggests that examining the comorbidity profiles of COVID-19 positive Veterans in conjunction with their clinical manifestations may yield more success in predicting health outcomes instead of focusing solely on comorbidities. Additional studies are warranted to elucidate the factors resulting in our observations.

Limitations

To ensure reliable longitudinal survival analysis while controlling for a wide variety of clinical parameters, a number of COVID-19 positive cases had to be excluded throughout the study period and during hypothesis testing. However, since the proportion of excluded cases were minor compared to the overall sample, exclusion bias likely played a marginal role in our findings. Additionally, this is a pilot-level study with a sample consisting of an overwhelming majority of males ($\sim$97%). Therefore, our findings must be cautiously interpreted in conjunction with existing literature and pending larger cohorts. Despite these limitations, our study provides important data to this limited body of literature and shares valuable information regarding COVID-19 infections among this understudied population.

CONCLUSIONS

In our study, we found that age, cerebrovascular disease, initial disease severity, dyspnea, anorexia, and having two or more of the top 3 comorbidities and symptoms among our sample were independent predictors of death and poor survival. These risk factors may inform clinical management of COVID-19 infections among admitted VA patients. As our study adds to this limited body of literature, additional large-scale analyses on the U.S. Veteran population are merited to

confirm our findings and better understand the prognosis of COVID-19 among this vulnerable population.

CONFLICT OF INTEREST STATEMENT
The authors of this study have no conflict of interest to disclose.

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