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Short Communication

Age-Associated Predictors of Mortality among Patients with COVID-19 in New York City -

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ABSTRACT

Objectives: We tested the hypothesis that predictors of COVID-19 mortality would differ based on individuals' age groupings: 18-44 years; 45-64 years; and > 64 years, using data derived from one of the largest existing US-based case series of patients with COVID-19 in New York City and Long Island.

Methods: Data was retrieved from a large US-based case series of patients with COVID-19, captured from a quaternary academic health system in New York. Anaconda Python 3.7 was used to perform all analyses.

Results: As of May 24, 2020, 11,512 admitted patients were tested for COVID-19, with 4,446 (38.62%) being positive. Among patients testing positive, 959 (21.57%) died of COVID-19-related complications in the hospital. Overall, the median age of individuals testing positive was 54.1 years (SD, 18.9) and 47% were male. Cox proportional hazard models tested the relative importance of hypothesized demographic and medical mortality predictors within these three age groupings. Among 18-44-year-old patients, hypertension was a significant predictor of mortality. Among middle-aged patients (45-64 years), obesity was a significant predictor, and among those older than 64 years old, income, asthma, chronic obstructive pulmonary disease, coronary artery disease, and peripheral artery disease were significant predictors.

Conclusions: Evidence suggests individuals in all age groups are at risk for COVID-19-related adverse outcomes, but case fatalities are attributable to different risk factor profiles. Findings might aid in the development of both age-based risk-stratification strategies to inform decision-making about the management of patients with COVID-19 and rapid diagnostic and serological testing strategies.

Keywords: COVID-19; Predictors; Age; Mortality; Cardiovascular disease

INTRODUCTION

The first wave of scientific reports characterizing individuals seeking care for their COVID-19-related symptoms painted a grim picture for older adults with pre-existing conditions [1-4]. Indeed, early evidence from Wuhan (China) strongly suggested that individuals with obesity, hypertension, hyperlipidemia, and diabetes had elevated risks of severe COVID-19 presentation [4]. Several recent reports from New York, an important epicenter of the pandemic in the United States, have supported early findings that increasing age and comorbidities were strong predictors of severe COVID-19 infection and related-critical illness. Additionally, individuals' pre-existing health conditions also had a greater likelihood of death due to medical complications associated with the disease [5-7].

New data have emerged suggesting adverse effects of COVID-19 are observed across the lifespan, but factors associated with case fatalities are likely divergent [2,8]. In this report, we endeavored a closer examination of age-associated factors predicting mortality resulting from COVID-19-related complications using data derived from one of the largest existing US-based case series of patients with COVID-19, captured from a large quaternary academic health network covering a large catchment area from New York City and Long Island [4,9]. Specifically, we tested the hypothesis that predictors of COVID-19 mortality would differ based on individuals' ages at the time of hospitalization using three age groupings: 18-44 years; 45-64 years; and >64 years.

METHODS

We analyzed data from an integrated electronic health record system (Epic Systems, Verona, WI), including inpatient and outpatient visits from March 1, 2020, to May 24, 2020. Patients were tested for COVID-19 if they presented to the emergency department with any of the following complaints: fever, cough, shortness of breath, fatigue, gastrointestinal complaints, exposure to someone testing positive for COVID. COVID-19 testing relied on the SARS-CoV2 Xpert Xpress assay in the Cepheid GeneXpert instruments. Details regarding procedures for defining positive COVID-19 cases have been published elsewhere [9]. For our analyses, EHR queries yielded these variables: age at the time of testing, sex, race/ethnicity aggregated as non-Hispanic black, Asian and Hispanic referenced to non-Hispanic white; smoking history, cardio-metabolic conditions (e.g., hypertension, hyperlipidemia, diabetes, obesity, peripheral artery disease, and coronary artery disease); a history of pulmonary disease (e.g., chronic obstructive pulmonary disease, sleep apnea, or asthma); and autoimmune disease and cancer. Other factors derived from EHR queries included upper and lower airway respiratory conditions such as Chronic Obstructive Pulmonary Disease (COPD), asthma, and sleep apnea; COPD was defined as the presence of chronic bronchitis or emphysema [10]. For patients with COPD or asthma, an effort was made to cross-validate the history of these medical conditions with reported COPD or asthma treatment.

Predictors in our analyses were selected based on prior clinical research on COVID-19 patients. Demographic factors included age, sex, and race/ethnicity. Median household income quartiles based on the patient's 5-digit ZIP code were included as a proxy of socioeconomic status (25th percentile $34,361; 50th percentile $37,580; 75th percentile $41,328) [11]. Medical factors described above were also included in the multivariate-adjusted Cox proportional model, assessing the strength of each predictor associated with COVID-19 mortality. Anaconda Python 3.7 was used to perform all analyses and examine derived associative plots. This study was approved by the NYU Grossman School of Medicine Institutional Review Board, which granted both a waiver of informed consent and a waiver of the Health Information Portability and Privacy Act.

RESULTS

As of May 24, 2020, 11,512 patients admitted to the hospital were tested for COVID-19, with 4,446 (38.62%) being positive. Among patients testing positive, 959 (21.57%) died of COVID-19-related complications at the hospital. The present analyses focused on the age-associated factors predicting mortality among patients with a COVID-19 diagnosis (Supplemental Data). Overall, the median age of individuals testing positive was 54.1 years (SD, 18.9), and 47% were of the male sex.

Cox proportional hazard models tested the relative importance of each factor in predicting mortality within the following age groupings: 18-44 years; 45-64 years; and >64 years. In the models, time-to-discharge was calculated using the initial admission and discharge dates. These events were defined based on the patient state (alive or deceased) at discharge. No information regarding post-discharge events was available during queries. We used Random-Forest modeling to select which factors should be entered in the Cox models using their clinical importance based on previous research

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and feature importance in building parsimonious prediction model; all variables met the threshold filter, with feature importance of 0.03 [12].

Among 18-44 year-old patients, the presence of hypertension [HR = 3.19, 95% CI = 1.38-7.36, $p < 0.01$] was a significant predictor of mortality; race/ethnicity and obesity bordered significance [HR = 3.60, 95% CI = 1.00-12.93, $p = 0.06$ and HR = 2.12, 95% CI = 0.90-5.01, $p = 0.09$, respectively]. Among middle-age patients (45-64 years), the presence of obesity [HR = 1.45, 95% CI = 1.10-1.91, $p < 0.01$] was a significant predictor of mortality; individuals of the female sex tended to be at lower risk [HR = 0.76, 95% CI = 0.55-1.05, $p = 0.09$]. Lastly, among patients older than 64 years old, those of lower income [HR = 1.24, 95% CI = 1.04-1.48, $p < 0.01$] or with a diagnosis of chronic obstructive pulmonary disease [HR = 1.37, 95% CI = 1.09-1.73, $p < 0.01$], coronary artery disease [HR = 1.21, 95% CI = 1.01-1.46, $p < 0.05$], or peripheral artery disease [HR = 1.38, 95% CI = 1.07-1.78, $p < 0.01$] were at significantly greater risk of mortality; of note, those without asthma [HR = 0.77, 95% CI = 0.59-0.99, $p < 0.01$] were at significantly lower risk of mortality (Table 1).

Table 1: Factors associated with mortality among patients with COVID-19 by age groupings: 18-44 years; 45-64 years; and > 64 years.

Model I (14-44 years, *n* = 694)	HR	95% CI Lower	95% CI Upper	p
Race/Ethnicity	3.60	1.00	12.93	0.06
Female Sex	0.48	0.18	1.27	0.14
Low Income	1.91	0.84	4.37	0.12
Obesity	2.12	0.90	5.01	0.09
Smoking	1.02	0.13	8.09	0.98
Autoimmune Disease	-	-	-	-
Asthma	0.60	0.16	2.34	0.47
Sleep Apnea	1.04	0.22	4.82	0.96
Chronic Obstructive Pulmonary Disease	-	-	-	-
Hypertension	3.19	1.38	7.36	0.01
Diabetes	0.59	0.20	1.72	0.34
Hyperlipidemia	0.76	0.24	2.44	0.64
Cancer	1.98	0.40	9.69	0.40
Coronary Artery Disease	-	-	-	-
Peripheral Artery Disease	-	-	-	-
Model II (45-64 years, *n* = 1,394)				
Race/Ethnicity	1.10	0.83	1.46	0.51
Female Sex	0.76	0.55	1.05	0.09
Low Income	1.24	0.92	1.67	0.16
Obesity	1.45	1.10	1.91	0.01
Smoking	1.30	0.64	2.62	0.47
Autoimmune Disease	0.67	0.30	1.51	0.33
Asthma	0.98	0.62	1.53	0.91
Sleep Apnea	0.88	0.53	1.45	0.61
Chronic Obstructive Pulmonary Disease	1.21	0.56	2.62	0.63
Hypertension	0.91	0.68	1.23	0.55
Diabetes	1.06	0.78	1.42	0.72
Hyperlipidemia	0.81	0.59	1.11	0.19
Cancer	1.45	0.90	2.32	0.13
Coronary Artery Disease	1.21	0.75	1.94	0.43
Peripheral Artery Disease	1.07	0.54	2.12	0.84
Model III (> 64 years, *n* = 2,057)				
Race/Ethnicity	1.08	0.93	1.26	0.32
Female Sex	1.00	0.86	1.17	0.98
Low Income	1.24	1.04	1.48	0.01
Obesity	0.91	0.77	1.07	0.24
Smoking	0.91	0.64	1.30	0.62
Autoimmune Disease	0.86	0.59	1.26	0.44
Asthma	0.77	0.59	0.99	0.04
Sleep Apnea	0.86	0.62	1.19	0.37
Chronic Obstructive Pulmonary Disease	1.37	1.09	1.73	0.01
Hypertension	1.02	0.84	1.24	0.81
Diabetes	0.92	0.78	1.08	0.32
Hyperlipidemia	0.96	0.81	1.14	0.67
Cancer	1.07	0.89	1.3	0.47
Coronary Artery Disease	1.21	1.01	1.46	0.04
Peripheral Artery Disease	1.38	1.07	1.78	0.01

Multivariate-adjusted Cox proportional modeling predicting mortalityassociated with covid-19. Race/Ethnicity was coded as non-Hispanic black, Asian, and Hispanic referenced to non-Hispanic white. Household income based on zip code was used to categorize the patients by median income quartiles; 25th percentile $34,361; 50th percentile $37,580; 75th percentile $41,328); the lowest quartile was entered as a predictor in the models. The concordance index for each Cox PH model was: 0.81, 0.55, and 0.57, respectively. Chronic Obstructive Pulmonary Disease, Peripheral Artery Disease, Autoimmune Disease, and Coronary Artery Disease were excluded from model 1 because of insufficient cases.

DISCUSSION

In this consecutive case series of patients presenting at our academic health system in New York City, age was a significant predictor of COVID-19-related mortality based on our preliminary analysis, [1-3] prompting the need to explore further other age-related contributory factors. Based on our multivariate models (Table 1), we observed that age alone seems insufficient to characterize fully the patients who are at risk of COVID-19-related mortality. Results of our analyses are consistent with our hypothesis that the predictors of COVID-19 mortality differed based on individuals' age groupings: 18-44 years; 45-64 years; and >64 years, favoring the need for a nuanced approach when ascertaining predictors of COVID-19 mortality.

Results of our multivariate-adjusted analyses revealed differing factors are associated with COVID-19 mortality within each age grouping, as presently construed. Specifically, our models revealed that among young patients (18-44 years), those with a diagnosis of hypertension seem at the greatest mortality risk. Among middle-aged patients (45-64 years), those who were obese had the highest mortality risk, whereas among older adults (> 64 years), those with lower income or with a diagnosis of chronic obstructive pulmonary disease, coronary artery disease, or peripheral artery disease were at the greatest risk, but those without a history of asthma were at a lower risk.

Generally, our data are consistent with converging evidence that individuals in all age groups are at risk for COVID-19-related adverse outcomes [2,13,14]. However, it seems evident that case fatalities might be attributable to different risk factor profiles. Our data are in line with published reports that have emerged recently, suggesting multiple adverse effects of COVID-19 infection across the lifespan [8,10,15,16]. New COVID-19 cases observed from other regions of the United States suggest alarming increases in COVID-19 infection among individuals of younger ages, although the clinical course and seroconversion seem different across the lifespan [17,18]. It is worth noting that while infections are common among individuals of younger ages, they may not present to the hospital because they tend to be asymptomatic (10-90%) [3]. We posit that these findings might aid in the development of both age-based risk-stratification strategies to inform decision-making about the management of patients with

COVID-19 and rapid diagnostic and serological testing strategies aiming at high-risk groups [19-21].

DISCLOSURE OF INTEREST

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