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CHEST

Male Sex, Severe Obesity, Older Age, and Chronic Kidney Disease Are Associated With COVID-19 Severity and Mortality in New York City

To the Editor:

The pathophysiology of the acute respiratory syndrome in the setting of coronavirus disease 2019 (COVID-19) is not yet fully understood.[1] Differences in severity and fatality outcomes according to patient's sex have been noted across multiple early pandemic outbreak areas, such as China[2] and Italy.[3] Studies performed in the United States have examined predictors of mortality and severity; however, they included a few hundred patients[4] or were focused on time periods early in the COVID-19 outbreak, and confounders were not properly addressed with multivariate analyses.[5,6] Here we assess differences in COVID-19 severity between male and female patients while accounting for a large number of demographic and clinical covariates in New York City by investigating both initial presentation and mortality among hospitalized patients with COVID-19.

Methods

Anonymous data from the Mount Sinai Hospital System (MSHS) COVID-19 registry were downloaded from February 29, 2020 to May 19, 2020, and ED and inpatient encounters were selected. The dataset contained patient demographics, comorbidities, vital signs, and outcomes. COVID-19 results were confirmed using reverse transcription polymerase chain reaction on nasopharyngeal swabs. Ever smokers were defined as current and former smokers. Hypoxemia was determined as a peripheral oxygen saturation measurement at or below 92%.[7] Sepsis was determined using the Systemic Inflammatory Response Syndrome criteria.[8] The main outcomes in this study were (1) mortality and (2) clinical presentation at admission (peripheral O_2 saturation, sepsis). χ^2 tests were performed for univariate analyses, and multivariate stepwise logistic regression models were performed for multivariate analyses. Demographic and clinical variables to be included in the model were selected according to a priori knowledge of their association with COVID-19 mortality and severity, as well as according to results of univariate analyses (e-Table 1). All analyses were performed in SAS v9.4. This study was reviewed by the Institutional Review Board of Mount Sinai and considered exempt.

Results

Patient Characteristics

There were 43,564 patients who had a COVID-19-related encounter, excluding telehealth and rapid testing center visits. Of these, 4,062 patients admitted with confirmed COVID-19 were selected. Most patients were males (n = 2,333; 57.4%), and a larger proportion of men were <40 years old (7.1% vs 5.8%) and between 40 and 69 years old (53.0% vs 41.1%; $P < .0001$) compared with women of those age groups (Table 1). Males were less likely to report a history of diabetes (22.5% vs 25.4%; $P = .032$), hypertension (32.4% vs 39.0%; $P < .0001$), BMI ≥ 35 kg/m^2 (12.1% vs 23.8%; $P < .0001$), and more likely to report coronary artery disease (13.9% vs 12.4%; $P = .18$), chronic kidney disease (12.3% vs 11.2%; $P = .29$), and to be ever smokers (38.7% vs 25.9%; $P < .0001$) than females.

Clinical Presentation and Mortality

In total, 1,190 patients (29.3%) died (males, 29.8% vs females, 28.6%; $P = .4216$). At multivariable analysis, male sex was associated with a significantly increased risk of mortality compared with females (OR_{adj}, 1.37; 95% CI, 1.15-1.64 vs female) (Table 2). Older age, chronic kidney disease (CKD), and BMI ≥ 35 kg/m^2 were also significantly associated with increased risk of death (Table 2).

Males also were more likely to present with sepsis (62.9% vs 54.3%; $P < .0001$) and lower O_2 saturation on admission (≤92% O_2 saturation: males, 82.6%; females, 78.9%; $P = .0026$). At multivariate analysis (Table 2), male sex, older age, history of cancer, and a BMI ≥ 35 kg/m^2 were significantly associated with decreased O_2 saturation on presentation. A history of cancer was significantly associated with higher odds of sepsis on initial presentation, and a significant interaction between age and sex was observed ($P < .05$). Males in each age category were more likely to present with sepsis than were female subjects, although the association was significant for the age groups < 40 years and 40 to 69 years.

TABLE 1] Patient Characteristics (N = 4,062)

Variable		Male n = 2,333 (57.4%)	Female n = 1,729 (42.6%)	*P* Value
Race	White	588 (25.2%)	402 (23.2%)	<.0001
	Black	513 (22.0%)	501 (29.0%)	
	Other/unknown	1,232 (52.8%)	826 (47.8%)	
Age, y	<40	166 (7.1%)	101 (5.8%)	<.0001
	40-69	1,237 (53.0%)	710 (41.1%)	
	≥70	930 (39.9%)	918 (53.1%)	
Smoking[a]	Ever	666 (38.7%)	356 (25.9%)	<.0001
	Never	1,056 (61.3%)	1,018 (74.1%)	
BMI ≥ 35 kg/m^2[b]	Yes	253 (12.1%)	370 (23.8%)	<.0001
	No	1,843 (87.9%)	1,182 (76.2%)	
Hypertension	Yes	756 (32.4%)	675 (39.0%)	<.0001
	No	1,577 (67.6%)	1,054 (61.0%)	
Diabetes	Yes	525 (22.5%)	439 (25.4%)	.0325
	No	1,808 (77.5%)	1,290 (74.6%)	
COPD	Yes	103 (4.4%)	69 (4.0%)	.5068
	No	2,230 (95.6%)	1,660 (96.0%)	
Coronary artery disease	Yes	324 (13.9%)	215 (12.4%)	.1772
	No	2,009 (86.1%)	1,514 (87.6%)	
Chronic kidney disease	Yes	287 (12.3%)	194 (11.2%)	.2916
	No	2,046 (87.7%)	1,535 (88.8%)	
Asthma	Yes	68 (2.9%)	128 (7.4%)	<.0001
	No	2,265 (97.1%)	1,601 (92.6%)	
Cancer	Yes	167 (7.2%)	114 (6.6%)	.4831
	No	2,166 (92.8%)	1,615 (93.4%)	
Death	Yes	695 (29.8%)	495 (28.6%)	.4216
	No	1,638 (70.2%)	1,234 (71.4%)	
Sepsis[c]	Yes	1,467 (62.9%)	939 (54.3%)	<.0001
	No	866 (37.1%)	790 (45.7%)	
Minimum oxygen saturation at admission	≤92%	1,928 (82.6%)	1,364 (78.9%)	.0026
	>92%	405 (17.4%)	365 (21.1%)	

χ^2 tests were performed.

[a]Ever smoker defined as both current and former smokers, compared with never smokers. Nine hundred sixty-six patients were not asked about their smoking status or were missing smoking status.

[b]Four hundred fourteen patients were missing BMI.

[c]Sepsis was determined by using the Systemic Inflammatory Response Syndrome criteria, with septic patients fulfilling two or more of the following: heart rate ≥ 90 beats/min, maximum temperature measured ≥ 38 °C, respiratory rate > 20 breaths/min, WBC count ≥ 12,000/μL or <4,000/μL.

Discussion

This analysis identifies critical predictors of severity and mortality among hospitalized COVID-19 patients within the MSHS, which serves a diverse population and geographic area in NYC. Male patients, older patients, patients who were severely obese, and patients with comorbidities were most at risk for adverse outcomes and mortality, concurrent with data from China, Italy, and the United States.[2-6] As the individual immunoresponse decreases and becomes less efficient with increasing age, the adverse outcomes in older patients noted here are not unexpected.[9]

We report here a 37% increase in risk of death in male vs female patients with COVID-19; females in general are known to mount stronger innate and adaptive immune responses, and they may have some baseline increased capacity to clear COVID-19 infection.[10] The result confirms a previous observation, on a much smaller New York City sample, that males experience more severe COVID-19 clinical course and worse outcomes.[4]

TABLE 2] Predictors of Mortality, Low O_2 Saturation, and Sepsis Among MSHS COVID-19 Patients

Relative Odds of Death[a]		Relative Odds of Hypoxemia at Admission[b]		Relative Odds of Sepsis at Admission[c]		
Variable	OR_{adj} (95% CI)	Variable	OR_{adj} (95% CI)	Variable	OR_{adj} (95% CI)	
Sex: Male vs female	1.37 (1.15-1.64)	Sex: Male vs female	1.37 (1.13-1.66)	Sex* Age[c]	Females	Males
Age, y		Age, y		Age, y		
<40	1 (ref)	<40	1 (ref)	<40	1 (ref)	3.50 (1.79-6.82)
40-69	8.45 (3.43-20.81)	40-69	2.14 (1.52-3.01)	40-69	1.26 (0.78-2.05)	1.84 (1.15-2.80)
≥70	24.21 (9.83-59.63)	≥70	2.90 (2.03-4.15)	≥70	0.90 (0.56-1.46)	1.05 (0.65-1.70)
History of CKD, y/n	1.38 (1.10-1.73)	Race		Race		
BMI ≥ 35 kg/m^2, y/n	1.53 (1.21-1.94)	White	1 (ref)	White	1 (ref)	
		Black	0.59 (0.45-0.77)	Black	1.05 (0.85-1.30)	
		Other/unknown	0.86 (0.67-1.10)	Other/unknown	1.41 (1.17-1.70)	
		History of COPD, y/n	1.62 (0.98-2.70)	History of cancer, y/n	1.53 (1.17-2.00)	
		History of cancer, y/n	1.44 (1.00-2.06)	History of hypertension, y/n	0.88 (0.75-1.03)	
		BMI ≥ 35	1.72 (1.31-2.26)			

CKD = chronic kidney disease.

[a]Stepwise logistic regression model performed. Race, smoking status, hypertension, history of asthma, COPD, diabetes, HIV, cancer were originally included in the model and were removed; the final model was adjusted for sex, age, history of CKD, and BMI.

[b]Stepwise logistic regression model performed. Smoking status, hypertension, asthma, CKD, and HIV were originally included in the model and were removed. The final model was sex, age, race, history of COPD, history of cancer, and BMI. Hypoxemia was defined as patients with ≤92% peripheral O_2 saturation.

[c]Stepwise logistic regression model performed. Smoking status, asthma, COPD, CKD, HIV, and obesity were originally included in the model and were removed. The final model was adjusted for sex*age, age, race, history of cancer, and history of hypertension. The age*sex interaction term ($P < .05$) and the sex and age group interaction terms (40-69 vs <40 years; $P = .0182$; ≥70 vs <40 years, $P = .0018$) were statistically significant.

Here we also report that sepsis and hypoxemia at admission are early clinical indicators of subsequent mortality from COVID-19, and that patients who were male, older, and had comorbidities were more likely to present with these clinical characteristics. These results add to the conversation about predictors of worse outcomes in COVID-19 patients, and point at male patients, as well as those who are older, those who are severely obese, and those with comorbidities as those likely at greatest risk of COVID-19 severity and fatality. These groups must be considered when planning the immediate and long-term health system response to the pandemic.

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Additional information: The e-Table can be found in the Supplemental Materials section of the online article.

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