Heart Disease, Advanced Age, Minority Race, and Hispanic Ethnicity Are Associated With Mortality in COVID-19 Patients

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ABSTRACT

Background: The objective of this study was to determine the associations between heart disease, obesity, and demographic factors and increased COVID-19 mortality.

Methods: We extracted deidentified patient-level data from the Froedtert Health System and Children's Hospital of Wisconsin and used descriptive statistics and multivariable logistic regression to characterize relationships between heart disease, obesity, age group, sex, race and ethnicity, and mortality following COVID-19 diagnosis.

Results: We found heart disease (adjusted odds ratio [AOR] 2.85; 95% CI, 2.11-8.83) and other demographic factors are significant predictors of increased mortality in COVID-19 patients. However, obesity was not a significant predictor of mortality (AOR 1.04; 95% CI, 0.53- 3.10).

Discussion: These unique results indicate some comorbid conditions and patient demographics contribute more strongly to mortality in COVID-19 patients.

INTRODUCTION

COVID-19, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is an ongoing global pandemic since its emergence in late 2019. While vaccines against SARS-CoV-2 are now widely available, the virus continues to spread, resulting in a profound impact on our health care system. Evidence suggests SARS-CoV-2 disproportionately affects certain populations, especially those with comorbid conditions[1-3] and some minority racial and ethnic groups.[4] While studies show comorbid conditions and patient demographics (eg, age, sex, race, ethnicity) are independently associated with poor health outcomes,[1-4] it is unclear which of these contributes more strongly to mortality in COVID-19 patients. Understanding these relationships is important for providing care as it informs which patients are potentially predisposed to poor outcomes following a COVID-19 diagnosis.

The purpose of this study was to explore the associations between mortality in COVID patients and comorbidities—specifically heart disease and obesity—and other demographic factors in a sample of patients in the Milwaukee, Wisconsin greater metropolitan area to understand further how the state has been affected.

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METHODS

Data Source

Data for this study were obtained from the Clinical and Translational Science Institute (CTSI) of Southeast Wisconsin's Clinical Research Data Warehouse (CRDW). The CRDW contains patient-level information for all encounters, including demographics, diagnoses, and diagnostic results. Institutional contributors to this database include the Froedtert Health System and Children's Hospital of Wisconsin (CHW). The database is maintained and updated weekly by the biomedical informatics team at the CTSI. TriNetX (a pharma-sponsored cohort query and analysis tool) was used to identify eligible patients. The Honest Broker data extraction tool was used to extract deidentified patient demographic data from TriNetX.

Patient Cohort

The study population included all patients with an encounter in the Froedtert Health System or CHW and a subsequent diagnosis

of COVID-19 based on International Classification of Diseases, Tenth Revision (ICD-10) code U07.1 between January 1, 2020 and November 18, 2020. Within this population, the 3 most common ICD-10 codes for each condition were used to classify individuals as having heart disease (I50, I50.9, I51.9) and/or obesity (E66, E66.9, E66.0).

Demographic data including shifted birth date, vital status (alive or deceased as of November 18, 2020), sex, race, and ethnicity, were extracted. Because of low numbers, individuals who identified as American Indian or Alaska Native, Native Hawaiian or other Pacific Islander, multiracial, other, and patients who chose not to disclose their race were grouped into a single "other" category.

Statistical Analysis

Descriptive statistics were used to report patient characteristics, including *t* tests to describe differences between alive and deceased patients for normally distributed data. Multivariate logistic regression was used to identify relationships between mortality and each predictor, while also controlling for each predictor analyzed. All statistics were performed using R version 1.31093. For all statistical analyses, 2-sided *P* values were used ($P < .05$ was statistically significant).

Table 1. Patient Characteristics

Characteristic	Alive (n=8567) No. (%)	Deceased (n=243) No. (%)	*P* value
Age			<0.001
0 – 24	1094 (12.8)	2 (0.8)	
25 – 44	3127 (36.5)	10 (4.1)	
45 – 64	2676 (31.2)	37 (15.2)	
65 – 84	1426 (16.6)	125 (51.4)	
85+	244 (2.8)	69 (28.4)	
Comorbidity			
Heart disease	883 (10.3)	126 (51.9)	<0.001
Obesity	2441 (28.5)	95 (39.1)	<0.001
Sex			<0.001
Female	5241 (61.2)	113 (46.5)	
Male	3325 (38.8)	130 (53.5)	
Race			0.04
White/Caucasian	5534 (65.2)	142 (58.4)	
Black/African American	2060 (24.3)	77 (31.7)	
Asian	206 (2.4)	8 (3.3)	
Other	684 (8.1)	16 (6.6)	
Ethnicity			0.52
Non-Hispanic	7725 (93.1)	19 (7.8)	
Hispanic	572 (6.9)	224 (92.2)	

T test for significance was performed to assess the difference between groups. $P < .05$ was considered significant.

RESULTS

Categorical Data

A total of 8810 patients who fit the inclusion criteria were seen in the Froedtert Health System or CHW between January 1, 2020 and November 18, 2020. Of the 8810 COVID-19 patients, 1009 (11.5%) were diagnosed with heart disease and 2536 (28.8%) were diagnosed with obesity. A total of 243 (2.8%) patients in the study died.

Among the COVID-19 patients in the study, deceased patients were more likely to be over 65, have heart disease and be obese (all $P < .0001$) (Table 1). Deceased patients also were more likely to be male ($P < 0.001$) and White or Caucasian ($P = 0.04$). However, it is important to note that 65% of all patients and 58.4% of all deceased patients were White or Caucasian. Additionally, only 24.5% of all patients in the study were Black or African American, yet 31.7% of all deceased patients were Black or African American.

Logistic Regression

In unadjusted analyses (Table 2), ages 45-64 years (odds ratio [OR] 7.56; 95% CI, 1.82-31.40), 65-84 years (OR 47.95; 95% CI, 11.85-194.05), and 85+ years (OR 154.68; 95% CI, 37.71-634.55) were significant predictors of death following a COVID-19 diagnosis. Additionally, both heart disease (OR 9.37; 95% CI, 7.22-12.17) and obesity (OR 1.61; 95% CI, 1.24-2.09), along with male sex (OR 1.81; 95% CI, 1.40-2.34) and Black or African American race (OR 1.46; 95% CI, 1.10-1.93), were significant predictors of death.

In the adjusted analysis (Table 2), obesity was no longer independently associated with increased mortality, while Asian race and Hispanic ethnicity became significant. The adjusted analysis showed similar increases in likelihood of death with increased age and male sex. Patients with heart disease were 2.85 times more likely (adjusted odds ratio [AOR] 2.85; 95% CI, 2.11-3.83) to die following a COVID-19 diagnosis than those without heart disease. Additionally, Black patients were 2.11 times more likely (AOR 2.11; 95% CI, 1.55-2.90) and Asian patients were 3.96 times as likely (AOR 3.96; 95% CI, 1.77-8.86) to die compared to White patients. Hispanic patients were 2.67 times more likely (AOR 2.67; 96% CI, 1.18-6.07) than non-Hispanic patients to die. The Figure shows a forest plot indicating the adjusted odds ratio for each predictor variable.

DISCUSSION

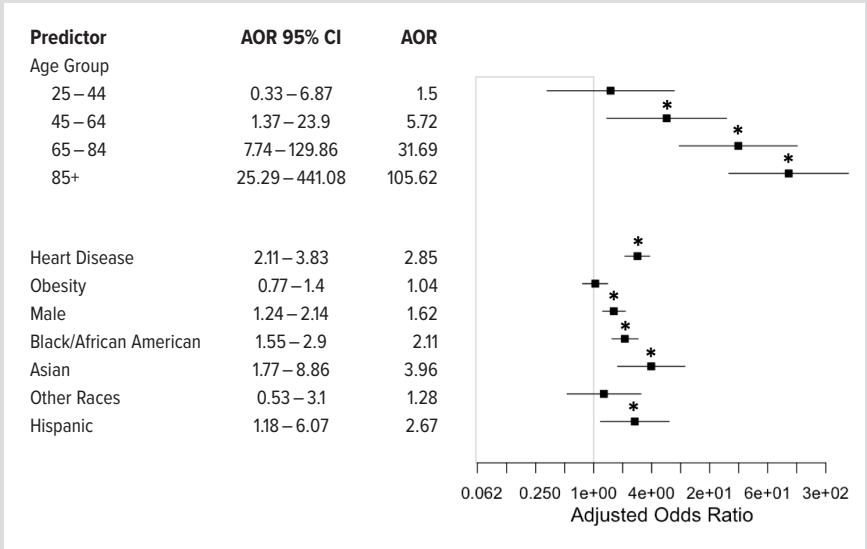
In this study, we found significant associations between heart disease, advanced age, male sex, minority race, and Hispanic ethnicity and increased mortality in COVID-19 patients. While other studies indicate obesity is associated with poor outcomes in COVID patients,[3,5] obesity was not a significant independent predictor of mortality when controlling for other factors in our study. These findings are unique, as we show underlying heart disease is more strongly associated with mortality than obesity in patients diagnosed with COVID-19. This suggests that comorbidities contribute in different ways to poor outcomes in COVID-19 patients, but much of these relationships is yet to be delineated. Characterizing and quantifying these relation-

Table 2. Logistic Regression Predicting Death Among COVID-19 Patients (N=8810)

Variable	Unadjusted *P* Value	Unadjusted Odds Ratio (95% CI)	Adjusted *P* value	Adjusted Odds Ratio (95% CI)
Age				
0 – 24	Referent		Referent	
25 – 44	0.47	1.75 (0.38 – 7.99)	0.6	1.50 (0.33 – 6.87)
45 – 64	< 0.05	7.56 (1.82 – 31.40)	0.016	5.72 (1.37 – 23.9)
65 – 84	< 0.001	47.95 (11.85 – 194.05)	< 0.001	31.69 (7.74 – 129.86)
85+	< 0.001	154.68 (37.71 – 634.55)	< 0.001	105.62 (25.29 – 441.08)
Comorbidity				
No heart disease	Referent		Referent	
Heart disease	<0.001	9.37 (7.22 – 12.17)	< 0.001	2.85 (2.11 – 3.83)
No obesity	Referent		Referent	
Obesity	< 0.001	1.61 (1.24 – 2.09)	0.78	1.04 (0.77 – 1.4)
Sex				
Female	Referent		Referent	
Male	< 0.001	1.81 (1.40 – 2.34)	<0.001	1.62 (1.24 – 2.14)
Race				
White/Caucasian	Referent		Referent	
Black/African American	< 0.05	1.46 (1.10 – 1.93)	< 0.001	2.11 (1.55 – 2.90)
Asian	0.26	1.51 (0.73 – 3.13)	< 0.001	3.96 (1.77 – 8.86)
Other	0.73	0.91 (0.54 – 1.54)	0.58	1.28 (0.53 – 3.10)
Ethnicity				
Non-Hispanic	Referent		Referent	
Hispanic	0.58	1.15 (0.71 – 1.84)	0.019	2.67 (1.18 – 6.07)

A univariate and multivariate logistic regression was performed with age group, underlying health condition, sex, and race as predictors of mortality following a COVID-19 diagnosis.

Figure. Forest Plot of Logistic Regression (N=8810)



Underlying health conditions and patient demographics as predictors of mortality following COVID-19 diagnosis. We report each predictor's adjusted odds ratio (AOR) (black boxes) and their respective 95% CI (bars) (*P< 0.05) compared to each predictor's referent.

ships indicates which comorbidities clinicians should be aware of while providing appropriate care for COVID patients.

Our patient demographic results are valuable as they indicate which characteristics in COVID patients more strongly contribute to mortality. While it is known that advanced age is associated with COVID-19 mortality,[3] our analyses show how different age groups are significantly affected. Similar to other studies, our findings show that Hispanic ethnicity and Black/African American and Asian races are associated with increased mortality in COVID-19 patients.[6-8] However, our findings uniquely depict how this relationship is stronger for Asian race. In fact, besides advanced age, Asian race is the strongest predictor of mortality in COVID-19 patients for this patient population.

In a similar study of the greater Milwaukee region, Egede and colleagues report Hispanic patients, but not non-Hispanic Black patients, were more likely to die from COVID-19 than White patients, and they propose this may be a product of Milwaukee's long history of structural racism.[7,9,10] We believe our results indicating Hispanic ethnicity and Asian race as significant predictors of death from COVID-19 could be similarly explained by structural racism. Our findings, in combination with those of Egede and colleagues,[7] amplify the need for future studies to investigate the roots of racial disparities in Milwaukee to develop alleviation strategies.

Limitations

One major limitation of our results lies in the data extraction method. We extracted data on patients with a COVID-19 ICD-10 code. Although all patients had COVID-19, it is unknown whether the viral infection itself was their final cause of death. Moreover, due to the nature of the CRDW data extraction from the electronic medical record, there may be patients in this data set who died but whose record was not updated at the time of data extraction.

Additionally, our use of COVID-19 diagnosis, rather than positive polymerase chain reaction (PCR) test, may be a limitation. We were unable to obtain data on patients who tested positive for SARS-CoV2 but never obtained a COVID-19 diagnosis, which includes patients who either recovered or developed worsening symptoms and died in their homes.

Another important limitation to consider is the nature of studying heart disease and obesity in the same multivariate model, as these conditions are often associated with one another thereby

explaining the lack of significance observed with obesity when examining both heart disease and obesity. This could be considered an overcorrection if heart disease is an intermediate step in the causal pathway from obesity to death, but this complex relationship has yet to clearly be delineated. Based on our unadjusted odds ratios, we conclude obesity is still associated with COVID-19 mortality, but the multivariate model indicates heart disease is a more significant predictor, warranting increased caution and vigilance in clinical scenarios.

Future Directions

In this study, we established heart disease as an important predictor of mortality in patients with COVID-19. However, there are many other chronic conditions that may increase susceptibility to death from COVID-19, such as diabetes, chronic respiratory illnesses, autoimmune diseases, and many others. Future studies should investigate the roles of other chronic conditions, in addition to heart disease and obesity, in COVID-19 mortality to better understand which conditions predispose patients to worse health outcomes. Moreover, they should incorporate additional demographic factors, such as income and ZIP code to improve our understanding of the social determinants of health as it pertains to COVID-19. Delineating these relationships will aid clinicians in considering factors that may predispose their patients to worse COVID-19 outcomes.

CONCLUSION

In this brief report, we have demonstrated heart disease, but not obesity, is significantly associated with mortality in COVID-19 patients. Additionally, we characterized the significant associations between advanced age, minority race, and Hispanic ethnicity and COVID-19 mortality. Future studies are needed that include more comorbid conditions, such as diabetes and chronic respiratory illnesses, and demographic factors, such as ZIP code and income.

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