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Association of obesity with illness severity in hospitalized patients with COVID-19: A retrospective cohort study

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Original Article

Association of obesity with illness severity in hospitalized patients with COVID-19: A retrospective cohort study

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ABSTRACT

Background: Although recent studies have shown an association between obesity and adverse coronavirus disease 2019 (COVID-19) patient outcomes, there is a paucity in large studies focusing on hospitalized patients. We aimed to analyze outcomes associated with obesity in a large cohort of hospitalized COVID-19 patients.
Methods: We performed a retrospective study at a tertiary care health system of adult patients with COVID-19 who were admitted between March 1 and April 30, 2020. Patients were stratified by body mass index (BMI) into obese (BMI $\geq$ 30 kg/m 2) and non-obese (BMI < 30 kg/m 2) cohorts. Primary outcomes were mortality, intensive care unit (ICU) admission, intubation, and 30-day readmission.
Results: A total of 1983 patients were included of whom 1031 (51.9%) had obesity and 952 (48.9%) did not have obesity. Patients with obesity were younger (P < 0.001), more likely to be female (P < 0.001) and African American (P < 0.001) compared to patients without obesity. Multivariable logistic models adjusting for differences in age, sex, race, medical comorbidities, and treatment modalities revealed no difference in 60-day mortality and 30-day readmission between obese and non-obese groups. In these models, patients with obesity had increased odds of ICU admission (adjusted OR, 1.37; 95% CI, 1.07–1.76; P = 0.012) and intubation (adjusted OR, 1.37; 95% CI, 1.04–1.80; P = 0.026).
Conclusions: Obesity in patients with COVID-19 is independently associated with increased risk for ICU admission and intubation. Recognizing that obesity impacts morbidity in this manner is crucial for appropriate management of COVID-19 patients.

Introduction

The outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first reported in Wuhan, China in December 2019 and has since led to the global coronavirus disease 2019 (COVID-19) pandemic, which has resulted in over 108 million cases and 2,300,000 deaths worldwide as of February 2021 [1]. As this disease has become more prevalent, public health interest has increased regarding vulnerable patient populations. Current guidelines from the Centers for Disease Control and Prevention suggest that individuals with cancer, chronic kidney disease, chronic obstructive pulmonary disease, history of solid organ transplant, cardiac conditions, sickle cell disease, type 2 diabetes, and obesity may be at increased risk for severe illness from COVID-19 [2].

Obesity has been studied extensively, as it is a modifiable risk factor with a high worldwide prevalence. An early study in China found that among 383 hospitalized patients with COVID-19, having overweight or obesity was associated with substantially increased risk for developing severe pneumonia [3]. A more recent retrospective study that evaluated factors associated with hospitalization at a large academic health system in New York City showed that obesity and age were the most important predictors for admission [4]. Although there has been a fair amount of recently published research studying the association between obesity and COVID-19, most of these studies have been relatively small in scale, and only a few have focused specifically on hospital-based outcomes. Because

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Michigan ranks fifth for obesity within the United States and was an epicenter of the COVID-19 pandemic during the initial infectious peak, our patient population provided a representative model to assess how COVID-19 is affecting individuals with obesity. We conducted this study to better understand the demographic characteristics of patients with obesity who were hospitalized with COVID-19 within our large metropolitan health system and to evaluate the link between obesity and adverse clinical outcomes in this population.

Materials and methods

Study design

This study was approved by the Henry Ford Health System Institutional Review Board. The study was a retrospective medical record review at a large tertiary care health system in Detroit, Michigan. Patients with SARS-CoV-2 infection confirmed by positive polymerase chain reaction testing of a nasopharyngeal specimen were included. The study cohort consisted of patients who were admitted and discharged to any of the 5 hospitals within the Henry Ford Health System between March 1 and April 30, 2020. Patients who were discharged directly from the emergency room or evaluated in outpatient clinics were not included in this study. If patients were admitted multiple times during the study interval, only the index admission following a positive COVID-19 test result was considered.

Data collection

A team of physicians performed a manual retrospective chart review on a standardized data collection form using the electronic medical record. Demographic data were collected from the electronic medical record including patient sex, age, race, body mass index (BMI), and current or prior cigarette use. Patients with obesity were stratified by obesity class based on BMI with class 1 obesity defined as BMI 30.0–34.9 kg/m^2, class 2 obesity defined as BMI 35.0–39.9 kg/m^2, and class 3 obesity defined as BMI equal to or greater than 40.0 kg/m^2. Primary outcomes included 60-day mortality, length of hospitalization, intensive care unit (ICU) admission, length of ICU admission, intubation, discharge home vs. hospice, and 30-day readmission. Mortality was calculated based on death of any cause either during the hospitalization or within 60 days of the patient's index admission.

In addition, the presence of baseline medical comorbidities including diabetes, sleep apnea, chronic obstructive pulmonary disease, asthma, hypertension, cardiovascular disease, and malignancy were recorded. Cardiovascular disease was defined by the presence of coronary artery disease, prior myocardial infarction, cerebrovascular disease, congestive heart failure, cardiac arrhythmia, or congenital heart disease.

Finally, data was collected on the use of various medical treatment modalities for COVID-19 including Hydroxychloroquine, Remdesivir, Tocilizumab, and plasmapheresis. During the study period, administration of Hydroxychloroquine 400 mg twice daily for 1 day followed by 200 mg twice daily for 4 days to complete a 5-day treatment course was considered standard of care at our institution for patients with an acute COVID-19 infection. A longer treatment duration was sometimes used in select patients based on the severity of their disease course. The other treatment modalities were considered experimental at the time of the study and therefore did not have a strict administration protocol in place. Tocilizumab and plasmapheresis were typically reserved for critically ill patients requiring ICU admission.

Statistical analysis

All continuous data were reported as mean ± standard deviation, while categorical data were reported as counts and column percentages. For continuous variables, univariate two-group comparisons were performed using independent 2-sample *t*-tests if the variable was normally distributed and Wilcoxon rank sum tests if the variable was not normally distributed. For categorical variables, univariate two-group comparisons were performed using chi-square tests when expected cell counts were > 5 and Fisher's exact tests when expected cell counts were < 5. Relative risk for the outcomes of interest were assessed using the log-binomial method. Multivariable logistic regressions were performed to examine the effect of obesity on the outcomes while adjusting for differences in patient demographics, medical comorbidities, and treatment modalities. Statistical significance was set at $P < 0.05$. All analyses were performed using SAS 9.4 (SAS Institute Inc., Cary, NC).

Results

A total of 1983 patients who tested positive for COVID-19 were hospitalized between March 1 and April 30, 2020 (993 [50.1%] men and 990 [49.9%] women), with a mean age of 63.8 ± 16.5 years. Of these patients, 1031 (51.9%) had obesity and 952 (48.9%) did not have obesity. The mean BMI for patients with obesity was 37.8 ± 7.5 and 24.9 ± 3.4 for patients without obesity. Among patients with obesity, 463 (45%) had class I obesity, 290 (28%) had class II obesity, and 278 (27%) had class III obesity. Table 1 shows baseline characteristics for patients with and without obesity.

Patients with obesity were younger (58.2 years vs. 69.9 years; $P < 0.001$), more likely to be female (55% women vs. 45% men; $P < 0.001$), and a higher proportion were African American (63% vs. 49%; $P < 0.001$) compared to those in the non-obese group. Patients with obesity were also more likely to be diabetic (41% vs. 35%; $P = 0.010$) and have obstructive sleep apnea (15% vs. 5%; $P < 0.001$), but were less likely to have cardiovascular disease (25% vs. 33%; $P < 0.01$) and malignancy (5% vs. 10%; $P < 0.01$).

Patients with obesity were more likely than non-obese individuals to receive treatment with Hydroxychloroquine (84% vs. 76%; $P < 0.001$) and Tocilizumab (6% vs. 3%; $P < 0.001$). There was no difference in the proportion of patients who received Remdesivir and Plasmapheresis treatment in each group.

Patients with obesity had a significantly lower 60-day mortality compared to patients without obesity (15% vs. 25%; $P < 0.001$). A total of 156 (15%) patients with obesity died and 1 patient in this group was discharged to hospice, while 242 (25%) patients without obesity died and 7 (1%) were discharged to hospice during the study period ($P < 0.001$). There was no significant difference for ICU admission (24% vs. 21%; $P = 0.078$), need for intubation (18% vs. 15%; $P = 0.157$), or 30-day readmission (9% vs. 11%; $P = 0.319$) in patients with and without obesity. Also, there was no significant difference in length of hospital stay (7.41 days vs. 7.44 days; $P = 0.913$) or length of ICU stay (8.87 days vs. 8.19 days; $P = 0.289$) between these two groups (Table 2).

When stratified by obesity class, the relative risk for 60-day mortality was significantly lower in the cohort of patients with obesity compared to the cohort of patients without obesity across all obesity classes (Table 3). There was a significant increased risk for ICU admission (relative risk 1.33; 95% CI 1.06−1.67) and intubation (relative risk 1.43; 95% CI 1.09−1.86) in patients with class III obesity compared to patients without obesity.

Table 1
Baseline patient characteristics.

Patient Characteristics (N = 1983)	Total (n = 1983)	Obese (n = 1031)	Non-Obese (n = 952)	*P*-value[a]
Age (years), mean ± SD	63.82 ± 16.55	58.20 ± 15.30	69.91 ± 15.68	< 0.001
Sex, N (%)				< 0.001
Female	990 (50%)	566 (55%)	424 (45%)	
Male	993 (50%)	465 (45%)	528 (55%)	
Race, N (%)				< 0.001
African American	1115 (56%)	647 (63%)	468 (49%)	
White	640 (32%)	283 (27%)	357 (38%)	
Asian	39 (2%)	11 (1%)	28 (3%)	
Hispanic	7 (0%)	5 (1%)	2 (0%)	
Other	92 (5%)	41 (4%)	51 (5%)	
Unknown	90 (5%)	44 (4%)	46 (5%)	
BMI (kg/m^2), mean ± SD		37.75 ± 7.48	24.87 ± 3.41	< 0.001
Obesity class, N (%)				
Non-obese (< 30)	952 (48%)	N/A	952 (100%)	N/A
Class 1 (30–34.9)	463 (23%)	463 (45%)	N/A	
Class 2 (35–39.9)	290 (15%)	290 (28%)	N/A	
Class 3 (>40)	278 (14%)	278 (27%)	N/A	
Medical comorbidities, N (%)				
Diabetes	760 (38%)	423 (41%)	337 (35%)	0.010
Sleep apnea	196 (10%)	151 (15%)	45 (5%)	< 0.001
COPD/Asthma	383 (19%)	213 (21%)	170 (18%)	0.114
Hypertension	1345 (68%)	697 (68%)	648 (68%)	0.825
Cardiovascular disease	572 (29%)	261 (25%)	311 (33%)	< 0.001
Malignancy	142 (7%)	50 (5%)	92 (10%)	< 0.001
Treatments, N (%)				
Hydroxychloroquine	1586 (80%)	862 (84%)	724 (76%)	< 0.001
Remdesivir	17 (1%)	10 (1%)	7 (1%)	0.569
Tocilizumab	84 (4%)	60 (6%)	24 (3%)	< 0.001
Plasmapheresis	5 (0%)	2 (0%)	3 (0%)	0.676

BMI, body mass index; COPD, chronic obstructive pulmonary disease; N/A, not applicable; SD, standard deviation.
[a] P-values reported using 2-sample *t*-test for age, Wilcoxon rank sum test for BMI, and chi-square or Fisher's exact test for other patient characteristics.

Table 2
Primary and secondary outcomes in obese and non-obese patients.

Patient Outcomes	Total (n = 1983)	Obese (n = 1031)	Not Obese (n = 952)	*P*-value[a]
60-day mortality, N (%)	398 (20%)	156 (15%)	242 (25%)	< 0.001
ICU admission, N (%)	448 (23%)	249 (24%)	199 (21%)	0.078
Intubation, N (%)	330 (17%)	183 (18%)	147 (15%)	0.157
30-day readmission, N (%)	156 (8%)	80 (9%)	76 (11%)	0.319
Length of hospital stay (days), mean ± SD	7.42 ± 6.28	7.41 ± 6.36	7.44 ± 6.19	0.913
Length of ICU stay (days), mean ± SD	8.54 ± 6.76	8.87 ± 6.61	8.19 ± 6.91	0.289

ICU, intensive care unit; SD, standard deviation.
[a] P values reported using Chi-square test and 2-sample *t*-test (length of hospital stay and length of ICU stay).

Table 3
Risk of morbidity and mortality in obese patients compared to non-obese patients stratified by obesity class.

	Relative Risk (95% CI)		
Outcome	Class I Obesity	Class II Obesity	Class III Obesity
60-day mortality	0.65 (0.51–0.82)	0.58 (0.43–0.78)	0.53 (0.38–0.72)
ICU admission	1.05 (0.85–1.30)	1.17 (0.92–1.48)	1.33 (1.06–1.67)
Intubation	0.97 (0.75–1.26)	1.18 (0.89–1.57)	1.43 (1.09–1.86)
30-day readmission	1.04 (0.73–1.48)	0.72 (0.45–1.17)	0.71 (0.43–1.16)

CI, confidence interval; ICU, intensive care unit.

Multivariable logistic regression models were performed to examine the effect of obesity on the odds of death, ICU admission, intubation, and 30-day readmission, while adjusting for other variables. When adjusted for differences in age, sex, race, medical comorbidities, and treatment modalities, obesity was not independently associated with 60-day mortality (adjusted odds ratio [OR] 1.10; 95% CI, 0.83–1.44; *P* = 0.512). The multivariable adjusted model showed that patients with obesity were at increased risk for ICU admission (adjusted OR, 1.37; 95% CI, 1.07–1.76; *P* = 0.012) and intubation (adjusted OR, 1.37; 95% CI, 1.04–1.80; *P* = 0.026), but not for 30-day readmission (adjusted OR 0.91; 95% CI, 0.62–1.35; *P* = 0.647) (Table 4). A secondary analysis was performed stratifying our cohort into males and females with obesity, again adjusting for other differences between these two groups (Table 5). This model showed that male patients with obesity did not have increased risk for any of the measured outcomes whereas females were at increased risk for ICU admission (adjusted OR, 1.53; 95% CI, 1.06–2.22; *P* = 0.025) and intubation (adjusted OR, 1.59; 95% CI, 1.04–2.44; *P* = 0.034) but not 60-day mortality or 30-day readmission.

Table 4
Multivariable logistic regression showing effect of obesity on morbidity and mortality.

Outcome	Odds Ratio	95% CI	*P*-value[a]
60-day mortality	1.10	0.83–1.44	0.512
ICU admission	1.37	1.07–1.76	0.012
Intubation	1.37	1.04–1.80	0.026
30-day readmission	0.91	0.62–1.35	0.647

ICU, intensive care unit.
[a] P values reported using a multivariable logistic regression model adjusting for differences in age, sex, race, medical comorbidities, and treatments received between the obese and non-obese groups.

Table 5
Multivariable logistic regression stratified by sex showing effect of obesity on morbidity and mortality.

	Males		*Females*	
Outcome	OR (95% CI)	*P*-value[a]	OR (95% CI)	*P*-value[a]
60-day mortality	1.18 (0.81, 1.73)	0.3834	1.05 (0.70, 1.58)	0.8181
ICU admission	1.28 (0.91, 1.79)	0.1547	1.53 (1.06, 2.22)	0.0247
Intubation	1.25 (0.86, 1.80)	0.2420	1.59 (1.04, 2.44)	0.0344
30-day readmission	0.98 (0.57, 1.69)	0.9382	0.86 (0.49, 1.49)	0.5180

OR, odds ratio; CI, confidence interval; ICU, intensive care unit.

[a] P values reported using a multivariable logistic regression model adjusting for differences in age, race, medical comorbidities, and treatments received between the obese and non-obese groups.

Discussion

In this study, we identified obesity to be an independent risk factor for ICU admission and intubation among patients hospitalized with COVID-19 but not associated with 60-day mortality or 30-day readmission rate. Interestingly, the link between obesity and illness severity was primarily observed in female patients but not in their male counterparts. Our study is amongst the largest to date evaluating the association between obesity and COVID-19 related morbidity and mortality within a single hospital system.

Our study cohort included patients who were hospitalized across multiple medical facilities within the larger Detroit metropolitan area, a region which has been heavily impacted by the COVID-19 pandemic. Almost 52% of patients in our study had obesity which is significantly higher than the prevalence of obesity within the Detroit metropolitan area (34.6%) based on data from 2014 [5]. Our patient population was notably unique compared to other studies in that it included a significant proportion of African Americans, who in prior studies have been shown to be disproportionately affected by COVID-19 [6–8]. While African Americans make up 14% of the population in the state of Michigan, there is a much higher population within the city of Detroit, where 79% of individuals are African American [9]. In our study, African Americans made up 56% of the study population and were also significantly more likely to have obesity compared to any other demographic group. Patients with obesity who were hospitalized with COVID-19 were also younger than their non-obese counterparts. This suggests that obesity may augment disease severity and potentially predispose younger individuals with obesity to require hospitalization. Our results corroborate findings from Kass et al., which showed an inverse correlation between age and BMI in a population of 265 patients hospitalized with COVID-19 [10].

Comparing mortality rate between the two groups, obesity was surprisingly associated with a significant decrease in 60-day mortality, and when patients were stratified by obesity class, the relative risk for death was significantly lower in the cohort of patients with obesity compared to the non-obese cohort across all obesity classes. This association was not seen with regard to length of hospitalization, ICU admission rate, length of ICU stay, need for intubation, and 30-day readmission rate, which were similar in both groups. To account for confounding variables, a multivariable logistic regression model was used to adjust for differences in patient age, sex, race, medical comorbidities, and treatment modalities between obese and non-obese groups. This multivariate analysis showed that obesity was not independently associated with decreased mortality; however, obesity was found to be a risk factor for ICU admission and intubation in hospitalized patients. To further examine this relationship, we stratified our cohort into male and female patients and the same outcomes were again assessed. Surprisingly, the association between obesity and increased illness severity (i.e., patients requiring ICU admission or intubation) and was only significant in the female population while male patients with obesity were not at increased risk for morbidity or mortality.

These conclusions highlight some interesting discussion points. Several smaller retrospective studies have reported similar results linking obesity to increased COVID-19 illness severity [11–13]. The etiologies for this are likely multifactorial, ranging from decreased cardiorespiratory reserve and thrombogenesis to hyperimmune-reactivity [14]. Some studies have suggested that the expression of angiotensin-converting enzyme 2, the functional receptor of SARS-CoV-2, is upregulated in adipocytes of patients with obesity, which turns adipose tissue into a potential viral reservoir [15], while others have implicated various cytokine pathways that may be amplified in these individuals [16]. Regardless of the underlying mechanism, there is strong evidence that individuals with obesity may be more likely to develop severe illness due to COVID-19. The predilection for female patients with obesity for having worse outcomes than males however has not been previously established. Most studies to date reporting COVID-19 outcomes in the general population, including one large meta-analysis looking at over 21,000 patients [17], have found that males tend to have a more severe disease and higher mortality compared to females. In comparison, literature on gender-based outcomes in patients with obesity is limited. One study which tracked 215 hospitalized COVID-19 patients with obesity found that mortality was significantly higher males [18], whereas a more recent study using data from a UK Biobank found that a higher BMI was associated with a stronger risk of COVID-19 mortality in women than men [19]. The findings from our study suggest that perhaps other factors including waist-to-hip ratio and distribution of adiposity may play a role in explaining the differences in outcomes between males and females.

Another question that arises then is why an association was not seen between obesity and mortality in our study. While some published studies have shown that there is a correlation between obesity and increased mortality in COVID-19 patients [18,20–22], most of these results have been based on smaller sample sizes and often were not adjusted for potential confounding variables. Our study suggests that although obesity may predispose individuals to more severe illness, overall mortality is unaffected when adjusted for patient age and other medical risk factors including diabetes and cardiovascular disease. Perhaps patients with obesity who are otherwise metabolically healthy are more likely to recover from a severe disease course, while those with other underlying risk factors are less likely to mount the same robust recovery.

Our study has a few notable limitations. Primarily, it may not be generalizable since our data were collected from a single large health system, and the demographics of the patient cohort may not be reflective of the general population. Likewise, the resources and workforce available at a tertiary care facility such as ours are not readily available elsewhere, and this may have affected patient outcomes. In addition, we only focused on evaluating patients who required hospital admission and did not capture the large proportion of patients who were managed in the outpatient setting or were discharged home from the emergency department. Other measurements of obesity such has waist circumference or waist-to-hip ratio would have been ideal to include in our analysis however these variables were unfortunately unable to be collected via retrospective chart review. Finally, as with any retrospective study, results may be subject to confounding bias from other unknown variables.

In conclusion, our study found that patients with obesity who were hospitalized with COVID-19, were younger, more likely to be female, and were more represented by African Americans. These patients were also more likely to have medical comorbidities such as diabetes and obstructive sleep apnea while less likely to have cardiovascular disease and malignancy. When adjusted for other potential confounding variables, obesity was independently associated with increased rate of ICU admission and intubation primarily in female patients. However, there was no association between obesity and overall mortality or hospital readmission rate in these otherwise healthy patients, suggesting that despite the more severe disease course, they are likely to recover compared to their counterparts with other risk factors. As healthcare providers continue to care for a diverse patient population during this pandemic, it is important to recognize that obesity can independently influence disease severity as this may help inform medical decisions about triaging, allocation of resources, and appropriate escalation of care.

Ethical statement

I have read and have abided by the statement of ethical standards for manuscripts submitted to the Obesity Research & Clinical Practice.

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Conflicts of interest

None.

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