Obesity

Association of Obesity with Disease Severity Among Patients with Coronavirus Disease 2019

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Objective: The aim of this study was to explore the potential association of obesity and other chronic diseases with severe outcomes, such as intensive care unit (ICU) admission and invasive mechanical ventilation (IMV), in patients hospitalized with coronavirus disease 2019 (COVID-19).
Methods: This study analyzed a retrospective cohort of 103 patients hospitalized with COVID-19. Demographic data, past medical history, and hospital course were collected and analyzed. A multivariate logistic regression analysis was implemented to examine associations.
Results: From February 17 to April 5, 103 consecutive patients were hospitalized with COVID-19. Among them, 44 patients (42.7%) were admitted to the ICU, and 29 (65.9%) required IMV. The prevalence of obesity was 47.5% (49 of 103). In a multivariate analysis, severe obesity (BMI ≥ 35 kg/m^2) was associated with ICU admission (adjusted odds ratio [aOR]: 5.39, 95% CI: 1.13-25.64). Moreover, patients who required IMV were more likely to have had heart disease (aOR: 3.41, 95% CI: 1.05-11.06), obesity (BMI = 30-34.9 kg/m^2; aOR: 6.85, 95% CI: 1.05-44.82), or severe obesity (BMI ≥ 35 kg/m^2; aOR: 9.99, 95% CI: 1.39-71.69).
Conclusions: In our analysis, severe obesity (BMI ≥ 35 kg/m^2) was associated with ICU admission, whereas history of heart disease and obesity (BMI ≥ 30 kg/m^2) were independently associated with the use of IMV. Increased vigilance and aggressive treatment of patients with obesity and COVID-19 are warranted.

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Study Importance

What is already known?

- Chronic conditions like diabetes, hypertension, obesity, heart and lung disease have been associated with coronavirus disease 2019 (COVID-19) severity.
- Evidence is limited, and the extent of these associations is not fully understood.

What does this study add?

- This US study shows that heart disease and obesity (BMI ≥ 30 kg/m^2) are independently associated with the use of invasive mechanical ventilation in patients with COVID-19.

How might these results change the direction of research or the focus of clinical practice?

- Individuals with BMI ≥ 35 kg/m^2, and especially those with heart disease, are at high risk for severe COVID-19.
- In areas with high prevalence of obesity, these findings can have a significant impact on the triaging and evaluation of patients.
- Studies should focus on mechanisms that explain why obesity is associated with increased COVID-19 severity, as well as streamlined prevention and treatment strategies for these patients.

Introduction

In late December 2019, a cluster of patients with pneumonia of unknown origin was first reported in Wuhan, China (1). Since then, coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has taken the world by storm, being officially declared a pandemic by the World Health Organization on March 11, 2020. Clinical manifestations of COVID-19 range from asymptomatic or mild infection to severe forms of disease that are life-threatening. Among other risk factors, chronic conditions such as chronic lung disease, cardiovascular disease, diabetes mellitus, and hypertension (2-4) seem to increase the risk for severe COVID-19 outcomes. In addition, although the role of obesity was initially neglected (5), recent reports (6,7) have found that obesity is associated with severe COVID-19 outcomes as well.

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In this study, we use data from the largest health care network in Rhode Island, with the aim of exploring the potential association of these chronic diseases with severe outcomes such as intensive care unit (ICU) admission and invasive mechanical ventilation (IMV) in patients hospitalized with SARS-CoV-2 infection.

Methods

Study design and patient selection

All consecutive adult (≥18 years old) patients who had a laboratory-confirmed (using a reverse transcriptase–polymerase chain reaction assay) SARS-CoV-2 infection and who were admitted to Rhode Island Hospital, The Miriam Hospital, or Newport Hospital in Rhode Island between February 17 and April 5, 2020, were considered eligible for inclusion. This study was a retrospective electronicchart review, and it was approved by the institutional review board of Rhode Island Hospital. A consent waiver was also obtained for the purposes of this study. This retrospective cohort study was performed in line with the Strengthening the Reporting of Observational Studies in Epidemiology statement (Supporting Information Table S1).

Data collection

Two independent investigators (MK, FS) extracted deidentified demographic, epidemiological, clinical, and laboratory data of interest. More specifically, they extracted the following variables: age, gender, race, smoking status, BMI, past medical history, and hospitalization course.

Study outcomes

Our primary outcome was to assess whether specific risk factors, namely age, race, gender, BMI, diabetes, hypertension, chronic heart disease, and chronic lung disease, are associated with ICU admission within the first 10 days of hospital admission with COVID-19. Our secondary objective was to assess whether the aforementioned factors are associated with the need for IMV during the first 10 days of hospital admission with COVID-19.

Statistical analysis

For the purposes of statistical analysis, we represented continuous measurements as medians (interquartile ranges), and we compared them using the Mann-Whitney Wilcoxon test. For categorical data, we used a 2-proportion z test to compare the difference in population proportions between patients admitted to the ICU and patients who did not require ICU admission. We also examined the association of ICU admission and the need for IMV with the following variables: age, race, gender, BMI, diabetes, hypertension, heart disease, and chronic lung disease. After examining the associations in a univariate logistic regression model, we performed multivariate logistic regression analysis, in which we included all of the variables in the same model. In addition, for the outcome of obesity, we show a model that adjusts for potential demographic confounders but does not include the other chronic disease variables. For our analyses, 95% CIs and P values are shown. All analyses were performed using Stata Statistical Software version 15.1 (StataCorp LLC, College Station, Texas).

Results

We identified 103 adult consecutive patients who were admitted with COVID-19 in our hospitals from February 17 to April 5. Patients baseline characteristics are depicted in Table 1. The median age of patients was 60 (52-70) years, and 63 patients (61.2%) were men. Among hospitalized patients with COVID-19, 42 were non-Hispanic white, 35 were Hispanic, 24 were non-Hispanic black, and 2 were non-Hispanic Asian. The most common comorbidity was hypertension (64.0%), followed by diabetes (36.8%) and heart disease (24.2%). The prevalence of obesity was 47.5% among hospitalized patients, 56.8% among patients requiring ICU admission, and 65.5% among patients who required IMV. During the first 10 days of their hospitalization, 44 out of 103 patients were admitted to the ICU, and 29 of them required IMV.

Both univariate and multivariate logistic regression analyses were used to examine the association of variables with ICU admission within the first 10 days of hospital admission (Table 2). In univariate models, none of the variables was associated with ICU admission. We performed a multivariate analysis (adjusted for age, gender, and race) to examine the association of obesity with ICU admission and found that severe obesity (≥35 kg/m^2) was associated with increased risk of ICU admission (adjusted odds ratio [aOR]: 6.16, 95% CI: 1.42-26.66). We then extended our multivariate model to include 4additional chronic diseases. Although diabetes, heart disease, and lung disease seemed to increase the risk of ICU admission, only severe obesity (≥35 kg/m^2) reached statistical significance (aOR: 5.39, 95% CI: 1.13-25.64).

As a secondary outcome, we examined factors associated with IMV within 10 days of hospital admission with COVID-19 (Table 3). In univariate models, preexisting heart disease and severe obesity were associated with the need for IMV. In a multivariate model examining the association of different BMI categories with IMV (after adjusting for age, gender, and race), severe obesity (≥35 kg/m^2) was associated with the need for IMV (aOR: 8.19, 95% CI: 1.36-49.13). In our expanded multivariate model, even though diabetes was associated with a trend for IMV, only the associations of heart disease and obesity with IMV reached statistical significance. More specifically, patients who needed IMV were more likely to have had a diagnosis of preexisting heart disease (aOR: 3.41, 95% CI: 1.05-11.06) or obesity (aOR of 6.85 and 9.99 for BMI 30-34.9 and ≥35 kg/m^2, respectively).

Discussion

We report on one of the first US cohorts examined for the association of obesity with the severity of COVID-19. We found that severe obesity (BMI ≥ 35 kg/m^2) was associated with ICU admission, whereas history of heart disease and obesity (BMI ≥ 30 kg/m^2) were independently associated with the use of IMV. A disproportionate impact of COVID-19 on patients with obesity should be anticipated because it has also been previously documented for different viral pathogens, including influenza (8-10). In particular, rates of hospitalizations and death due to the H1N1 influenza virus during the 2009 H1N1 pandemic were greater for both adults with obesity and adults with morbid obesity (11). Of note, death was associated with obesity (odds ratio: 3.1, 95% CI: 1.5-6.6) and morbid obesity (odds ratio: 7.6, 95% CI 2.1-27.9), even in patients who had no history of other medical conditions.

Given that the epicenters of COVID-19 are now North America and Europe, the impact of obesity on COVID-19 outcomes might become even more pronounced, as these 2 continents have the highest prevalence of obesity globally (12). Relatedly, the first results from France (7) and New York (6) are in concordance with our findings and they

TABLE 1 Baseline characteristics of patients hospitalized with COVID-19

	All ($n=103$)	ICU-admitted ($n=44$)	Non-ICU ($n=59$)
Age	60 (50-72)	61.5 (54.5-72.5)	57 (48-72)
Male	63 (61.2%)	29 (65.9%)	34 (57.6%)
Non-Hispanic white	42 (40.7%)	20 (45.4%)	22 (37.2%)
Non-Hispanic black	24 (23.3%)	11 (25.0%)	13 (22.0%)
Hispanic	35 (33.9%)	12 (27.2%)	23 (38.9%)
Non-Hispanic Asian	2 (1.9%)	1 (2.2%)	1 (1.6%)
Active smoker	12 (11.7%)	3 (6.8%)	9 (15.25%)
Former smoker	36 (34.9%)	17 (38.6%)	19 (32.2%)
Never smoker	55 (53.4%)	24 (54.5%)	31 (52.5%)
BMI < 25	19 (18.4%)	5 (11.3%)	14 (23.7%)
BMI 25-29.9	35 (33.9%)	14 (31.8%)	21 (35.5%)
BMI 30-34.9	22 (21.3%)	11 (25.0%)	11 (18.6%)
BMI ≥ 35	27 (26.2%)	14 (31.8%)	13 (22.0%)
Comorbidities			
Cancer	9 (8.7%)	6 (13.6%)	3 (5.0%)
Chronic renal	11 (10.6%)	4 (9.1%)	7 (11.8%)
Cirrhosis	3 (2.9%)	0	3 (5.0%)
Diabetes*	38 (36.8%)	21 (47.7%)	17 (28.8%)
Heart disease	25 (24.2%)	14 (31.8%)	11 (18.6%)
Hypertension	66 (64.0%)	31 (70.4%)	35 (59.3%)
Lung disease	20 (19.4%)	11 (25.0%)	9 (15.2%)
Transplant	2 (1.9%)	1 (2.2%)	1 (1.6%)

*P value = 0.025.
Continuous data: median (IQR), categorical data: n (%). Heart disease: heart failure, coronary artery disease, cardiomyopathy; lung disease: chronic obstructive pulmonary disease, asthma, interstitial lung disease, and pulmonary hypertension.
COVID-19, coronavirus disease 2019; ICU, intensive care unit; IQR, interquartile range.

TABLE 2 Association of different variables with ICU admission within 10 days of hospital admission with COVID-19

	Univariate		Multivariate[a]		Multivariate[b]	
	OR (95% CI)	*P* value	aOR (95% CI)	*P* value	aOR (95% CI)	*P* value
Age	1.02 (1.00-1.05)	0.067	1.03 (1.00-1.07)	0.016	1.03 (1.00-1.07)	0.059
Non-Hispanic white	ref		ref		ref	
Non-Hispanic black	0.93 (0.34-2.54)	0.889	0.86(0.29-2.56)	0.797	0.80 (0.26-2.45)	0.701
Hispanic	0.57 (0.23-1.45)	0.239	0.65 (0.24-1.76)	0.402	0.56 (0.19-1.58)	0.271
Female	ref		ref		ref	
Male	1.42 (0.63-3.19)	0.394	2.24 (0.86-5.78)	0.095	2.40 (0.87-6.64)	0.09
BMI < 25	ref		ref		ref	
BMI 25-29.9	1.87 (0.55-6.35)	0.318	2.14 (0.58-7.88)	0.250	2.27 (0.59-8.83)	0.235
BMI 30-34.9	2.80 (0.75-10.48)	0.126	2.56 (0.64-10.1)	0.100	2.65 (0.64-10.95)	0.178
BMI ≥ 35	3.02 (0.85-10.74)	0.088	**6.16 (1.42-26.66)**	**0.015**	**5.39 (1.13-25.64)**	**0.034**
Diabetes	2.26 (1.00-5.11)	0.051	N/A	N/A	1.91 (0.71-5.19)	0.202
Hypertension	1.64 (0.71-3.75)	0.246	N/A	N/A	0.79 (0.27-2.28)	0.663
Heart disease	2.04 (0.82-5.07)	0.126	N/A	N/A	1.52 (0.51-4.51)	0.448
Lung disease	1.85 (0.69-4.96)	0.22	N/A	N/A	1.50 (0.47-4.82)	0.495

Bold values: $P < 0.05$.
[a]Adjusted for age, race, and gender.
[b]Fully adjusted.
Heart disease: heart failure, coronary artery disease and cardiomyopathy; lung disease: chronic obstructive pulmonary disease, asthma, interstitial lung disease, and pulmonary hypertension.
aOR, adjusted OR; COVID-19, coronavirus disease 2019; ICU, intensive care until; N/A, not applicable; OR, odds ratio; ref, reference value.

TABLE 3 Association of different variables with need for IMV within 10 days of hospital admission with COVID-19

	Univariate		Multivariate[a]		Multivariate[b]	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Age	1.01 (0.98-1.04)	0.454	1.02 (0.99-1.06)	0.129	1.02 (0.98-1.06)	0.271
Non-Hispanic white	ref		ref		ref	
Non-Hispanic black	1.92 (0.65-5.71)	0.241	2.02 (0.63-6.47)	0.234	1.83 (0.55-6.11)	0.327
Hispanic	1.28 (0.46-3.55)	0.636	1.58 (0.53-4.74)	0.407	1.17 (0.36-3.82)	0.796
Female	ref		ref		ref	
Male	1.05 (0.44-2.55)	0.906	1.18 (0.43-3.19)	0.744	1.13 (0.32-3.40)	0.825
BMI < 25	ref		ref		ref	
BMI 25-29.9	2.52 (0.48-13.30)	0.277	2.64 (0.48-14.4)	0.262	3.70 (0.60-22.87)	0.159
BMI 30-34.9	4.86 (0.88-26.68)	0.069	5.28 (0.91-30.48)	0.063	**6.85 (1.05-44.82)**	**0.045**
BMI ≥ 35	**5.84 (1.12-30.55)**	**0.036**	**8.19 (1.36-49.13)**	**0.021**	**9.99 (1.39-71.69)**	**0.022**
Diabetes	2.38 (0.99-5.72)	0.054	N/A	N/A	2.13 (0.73-6.22)	0.168
Hypertension	1.35 (0.54-3.38)	0.518	N/A	N/A	0.47 (0.13-1.66)	0.242
Heart disease	**3.31 (1.28-8.57)**	**0.014**	N/A	N/A	**3.41 (1.05-11.06)**	**0.041**
Lung disease	1.49 (0.52-4.22)	0.45	N/A	N/A	0.76 (0.20-2.86)	0.687

Bold values: $P < 0.05$.
[a]Adjusted for age, race, and gender.
[b]Fully adjusted.
Heart disease: heart failure, coronary artery disease and cardiomyopathy; lung disease: chronic obstructive pulmonary disease; asthma, interstitial lung disease and pulmonary hypertension.
aOR, adjusted OR; COVID-19, coronavirus disease 2019; ICU, intensive care until; IMV, invasive mechanical ventilation; N/A, not applicable; OR, odds ratio; ref, reference value.

confirm this hypothesis. In a retrospective cohort study with 124 patients from France, Simonnet et al. (7) found that obesity prevalence was high among ICU-admitted patients (47.6%), whereas the aOR for IMV in patients with BMI ≥ 35 kg/m^2, compared with patients with normal weight, was 7.36 (1.63-33.14). Similarly, a study from New York with 3,615 patients by Lighter et al. () yielded results showing that, compared with individuals with BMI < 30, patients with BMI between 30 and 34.9 were 2.0 and 1.8 times more likely to be admitted to acute and critical care, respectively (6).

Although the exact mechanism by which obesity may contribute to severe COVID-19 outcomes is not yet defined, several parameters may play a role. First, patients with obesity have altered respiratory physiology, including decreased functional residual capacity and expiratory reserve volume, as well as hypoxemia and ventilation/perfusion abnormalities (13). In addition, obesity has been associated with impaired immunesystem surveillance and response (14), whereas the levels of angiotensin-converting enzyme 2 expression in adipose tissue, an enzyme for which SARS-CoV-2 shows high affinity, may also play a role and may need to be further studied (15).

Interestingly, we also found an association between preexisting heart disease (which is often associated with obesity as well (16)) and the need for IMV. Such findings are in agreement with previous reports, which have mentioned that patients with cardiovascular disease had an increased risk for severe outcomes, including death from COVID-19 (17). We should also mention that although chronic diseases like diabetes did not reach statistical significance in our analysis, previous reports have found an association with worse COVID-19 outcomes (18). Thus, future studies with more patients should reassess these findings.

Our study has some limitations that should be taken into consideration. Our CIs were relatively wide, likely because of the small sample size. In addition, there was low statistical power for testing interactions. Although the retrospective cohort study design used can estimate associations only, similar to a prospective design, our study does have the strength of certainty in regard to the temporal sequence of the exposures and outcomes.

In conclusion, our findings emphasize the need for early detection and aggressive treatment for patients with obesity and COVID-19, especially in countries like the United States, where the prevalence of obesity is more than 40% (19). We highlight the need for future studies that will assess the mechanisms behind increased COVID-19 severity in patients with obesity, as well as the need for streamlined prevention and treatment strategies for these patients.

Acknowledgments

The data sets generated and/or analyzed during the current study are not publicly available because of Health Insurance Portability and Accountability Act restrictions. Deidentified summary data are available from the corresponding author on reasonable request.

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Author contributions: All authors conceptualized and designed the study and participated in data interpretation. MK and FS participated in data collection and extraction. MK, FS, and EKM prepared tables and performed the statistical analysis. MK, FS, EKM, and GB drafted the initial manuscript. All authors reviewed and revised the manuscript. All authors read and approved the final manuscript as submitted and agree to be accountable for all aspects of the work, ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Supporting information: Additional Supporting Information may be found in the online version of this article.

References

1. Zhu N, Zhang D, Wang W, et al.; China Novel Coronavirus Investigating and Research Team. A novel coronavirus from patients with pneumonia in China, 2019. *N Engl J Med* 2020;382:727-733.
2. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72314 cases from the Chinese Center for Disease Control and Prevention [Published online February 24, 2020]. *JAMA*. doi:10.1001/jama.2020.2648
3. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet* 2020;395:1054-1062.
4. CDC COVID-19 Response Team. Preliminary estimates of the prevalence of selected underlying health conditions among patients with coronavirus disease 2019—United States, February 12–March 28, 2020. *MMWR Morb Mortal Wkly Rep* 2020;69:382-386.
5. Dietz W, Santos-Burgoa C. Obesity and its implications for COVID-19 mortality. *Obesity (Silver Spring)* 2020;28:1005.
6. Lighter J, Phillips M, Hochman S, et al. Obesity in patients younger than 60 years is a risk factor for Covid-19 hospital admission. *Clin Infect Dis* 2020:ciaa415. doi:10.1093/cid/ciaa415
7. Simonnet A, Chetboun M, Poissy J, et al.; COVID-19 and Obesity Study Group. High prevalence of obesity in severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) requiring invasive mechanical ventilation. *Obesity (Silver Spring)* 2020;28:1195-1199.
8. Kwong JC, Campitelli MA, Rosella LC. Obesity and respiratory hospitalizations during influenza seasons in Ontario, Canada: a cohort study. *Clin Infect Dis* 2011;53:413-421.
9. Moser JS, Galindo-Fraga A, Ortiz-Hernández AA, et al. Underweight, overweight, and obesity as independent risk factors for hospitalization in adults and children from influenza and other respiratory viruses. *Influenza Other Respir Viruses* 2019;13:3-9.
10. Maccioni L, Weber S, Elgizouli M, et al. Obesity and risk of respiratory tract infections: results of an infection-diary based cohort study. *BMC Public Health* 2018;18:271. doi:10.1186/s12889-018-5172-8
11. Morgan OW, Bramley A, Fowlkes A, et al. Morbid obesity as a risk factor for hospitalization and death due to 2009 pandemic influenza A(H1N1) disease. *PLoS One* 2010;5:e9694. doi:10.1371/journal.pone.0009694
12. World Health Organization. Prevalence of obesity among adults, BMI ≥ 30, age-standardized Estimates by WHO region. Accessed April 15, 2020. https://apps.who.int/gho/data/view.main.REGION2480A?lang=en
13. Parameswaran K, Todd DC, Soth M. Altered respiratory physiology in obesity. *Can Respir J* 2006;13:203-210.
14. Huttunen R, Syrjänen J. Obesity and the risk and outcome of infection. *Int J Obes (Lond)* 2013;37:333-340.
15. Kassir R. Risk of COVID-19 for patients with obesity. *Obes Rev* 2020;21:e13034. doi:10.1111/obr.13034
16. Van Gaal LF, Mertens IL, De Block CE. Mechanisms linking obesity with cardiovascular disease. *Nature* 2006;444:875-880.
17. Ruan Q, Yang K, Wang W, Jiang L, Song J. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. *Intensive Care Med* 2020;46:846-848.
18. Guo W, Li M, Dong Y, et al. Diabetes is a risk factor for the progression and prognosis of COVID-19. *Diabetes Metab Res Rev* 2020:e3319. doi:10.1002/dmrr.3319
19. Hales CM, Carroll MD, Fryar CD, Ogden CL. Prevalence of obesity and severe obesity among adults: United States, 2017-2018. *NCHS Data Brief* 2020:360. Accessed April 8, 2020. https://www.cdc.gov/nchs/products/databriefs/db360.htm