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Factors associated with inpatient complications among patients with obesity and COVID-19 at an urban safety-net hospital: A retrospective cohort study

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Abstract

Objective: Obesity increases morbidity and mortality from Coronavirus disease 2019 (COVID-19). This study characterized inpatient complications among patients with obesity and COVID-19—including myocardial infarction, renal failure requiring dialysis, stroke, secondary bacterial infection, and venous thromboembolism—and identified factors associated with developing at least one inpatient complication at a safety-net hospital with a diverse cohort.

Methods: A retrospective review was performed of all patients admitted for ≥ 3 days with COVID-19 between 16 March 2020, and 8 April 2020. Logistic regression identified factors associated with developing at least one COVID-19-related complication among patients with obesity (body mass index ≥ 30 kg/m²).

Results: 374 patients were included; 53.7% were classified as having obesity, 43.9% identified as Black, and 38.5% identified as Latino or Hispanic. Obesity was not associated with having at least one inpatient complication on multivariable analysis, but increased age (aOR 1.02, [95% CI 1.01–1.04], $p = 0.010$) and obstructive sleep apnea (aOR 2.25, [1.08–4.85], $p = 0.034$) were associated with this outcome.

Conclusions: Obesity was not associated with specified inpatient complications among patients with COVID-19 admitted to a health system caring for diverse patients. Future studies should incorporate larger cohorts and reflect newer treatment protocols.

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KEYWORDS

body mass index, complications, COVID-19, obesity, SARS-CoV-2

1 | INTRODUCTION

Coronavirus disease 2019 (COVID-19) has led to more than 5 million deaths worldwide and nearly one million deaths in the United States (US).¹ Obesity has been identified as an independent risk factor for poor outcomes in COVID-19 including intensive care unit (ICU) admission, intubation, and death.^{2,3} Less is known about other COVID-19 related complications including myocardial infarction, renal failure requiring dialysis, stroke, secondary bacterial infection, and venous thromboembolism (VTE) among people with obesity. The intersection of obesity and COVID-19 constitutes an important public health concern given an estimated 43% obesity prevalence in the US.^{4,5}

Increased adiposity generates a state of systemic low-grade inflammation that increases the risk of end-organ complications.⁶ The mechanisms underlying this predisposition are multifactorial and include endothelial damage and hypercoagulability.⁷ As a result, obesity predisposes to cardiovascular pathology including atherosclerosis, VTE, and cerebrovascular disease.⁸ Furthermore, increased adiposity disrupts innate and adaptive immunity and increases the risk of hospital-acquired infections.⁹ A growing body of evidence also correlates COVID-19 with cardiovascular complications among hospitalized patients. The combined effect of endothelial dysfunction and immune system dysregulation in both obesity and COVID-19 raises concern for inpatient complications in this high-risk population. However, few studies have clinically characterized this relationship. An in-depth understanding of inpatient complication profiles in patients with obesity may inform clinical decision-making and risk assessment during the COVID-19 pandemic.

Disparities in obesity and COVID-19 rates place specific groups at high risk for poor outcomes at the intersection of these two pandemics. For instance, the rate of obesity in 2017–2018 among non-Hispanic Black women was 56.9% compared to 39.8% among non-Hispanic White women.⁴ In addition, Black/African American, American Indian or Alaskan Native (AI/AN), and Latino or Hispanic patients diagnosed with COVID-19 are more likely to experience poor outcomes compared to patients who identify as White or Asian.¹⁰ Racial and ethnic disparities in disease burden extend to non-COVID-19 diagnoses. A recent study using provisional death certificate data from the Centers for Disease Control showed that among the 477,220 excess deaths in the United States between March and December 2020, non-COVID-19 excess deaths were 2 to 4 times higher in Black, AI/AN, and Latino patients during the study period, including deaths specifically due to heart disease and cerebrovascular disease.¹¹ However, little is known about complications acquired during the clinical course in a racially and ethnically diverse patient population.¹² The goal of this study was to characterize inpatient complications among patients with obesity and COVID-19

and compare inpatient complications between patients with and without obesity at an urban safety-net hospital that provides care to a racially and ethnically diverse patient population without regards for insurance status or ability to pay.

2 | METHODS

2.1 | Study design, site, and population

We performed a retrospective cohort study of all patients who were at least 18 years old, were admitted between 16 March 2020 and 8 April 2020, had symptoms of COVID-19, and had a positive SARS-CoV-2 reverse transcription polymerase chain reaction at Boston Medical Center (BMC), a 514-bed academic nonprofit safety-net hospital. BMC has a comprehensive weight center that integrates medical and surgical management. Approximately 230 patients are seen per week in clinic, and an estimated 24% of BMC patients with obesity have been evaluated at the center (personal communication). We excluded patients who had been admitted for less than 3 days to allow time for the development of inpatient complications. COVID-19 treatment protocols at BMC during the study timeframe have been described previously and included a protocol for early identification of patients at risk for severe COVID-19 and administration of the immunomodulators tocilizumab, sarilumab, and anakinra.¹³

2.2 | Data collection

We manually abstracted patient demographics, medical history (defined by International Classification of Disease 10 codes), baseline laboratory values, medical interventions, and clinical outcomes from the electronic medical record. We recorded clinical variables to the point of hospital discharge, transfer to another facility, or death.

Since blood gases were not routinely collected on admission, oxygenation status was estimated using the ratio of peripheral capillary oxygen saturation to fraction of inspired oxygen (SpO_2/FiO_2). Previous studies have indicated that this ratio approximates the ratio of partial pressure of oxygen to fraction of inspired oxygen (PaO_2/FiO_2).¹⁴

2.3 | Exposures and outcomes

Patients were categorized into 2 groups, BMI <30 kg/m² or BMI ≥30 kg/m². The primary outcome was the presence of at least one inpatient complication in patients with obesity. Complications of interest were chosen based on National Institutes of Health guidelines

at the time of database creation in April 2020.¹⁵ Inpatient complications were defined as new diagnoses acquired during the admission and included myocardial infarction, renal failure requiring dialysis, stroke, secondary bacterial infection, and VTE.

2.4 | Data analysis

We used descriptive statistics to characterize the patient population and linear regression to characterize inpatient complications between the two groups. We assessed the difference between patients with and without obesity using χ^2 test for categorical variables and t-test for continuous variables. We entered pre-specified demographic and medical history variables into a multivariable logistic regression to identify factors associated with at least one inpatient complication. We expressed associations from multivariable analysis using odds ratios with corresponding confidence intervals and p-values at $\alpha = 0.05$. A sensitivity analysis was conducted with age stratified into three groups (≤ 40 , 50–64, and ≥ 65 years) using ≤ 40 years as a reference group to identify factors associated with at least one inpatient complication. All statistical analyses were performed in R Core Team, 2020. The Boston University Medical Campus Institutional Review Board approved this study.

3 | RESULTS

We identified 374 patients who met inclusion criteria. The median (IQR) age was 57 (45–68) years with 57.8% male patients and 53.7% with obesity. The cohort consisted of 43.9% Black or African American and 38.5% Latino or Hispanic. The most common comorbidities were hypertension (62.8%) and diabetes (42.0%) (Table 1).

Patients with obesity were younger and more likely to be female when compared to patients without obesity (Table 1). They were also more likely to have chronic pulmonary disease and obstructive sleep apnea. Patients with obesity had lower baseline C-reactive protein and ferritin, although these findings were not statistically significant. They were more likely to receive immunomodulatory therapy for treatment of COVID-19-related clinical decline (43.8% vs. 29.5%). Patients with obesity were more often intubated (24.4% vs. 14.5%), but there were no differences in ICU admission, readmission, or in-hospital death between the two groups (Table 1). Secondary bacterial infection was the most common complication (44.4%), followed by bacteremia (4.5%), myocardial infarction (3.2%), and renal failure requiring dialysis (3.2%) (Table 2).

On multivariable analysis, obesity was not associated with developing any of the specified inpatient complications (aOR 1.19, [95% CI 0.73–1.93]). However, increased age (aOR 1.02, [1.01–1.04]) and obstructive sleep apnea (aOR 2.25, [1.08–4.85]) were associated with at least one inpatient complication (Table 3). Increased SpO₂/FiO₂ on admission (aOR 0.95, [0.92–0.98]) was inversely associated with inpatient complications. In a sensitivity analysis, obesity was not associated with hospital complications. SpO₂/FiO₂ on admission

(aOR 0.61, [0.43–0.82]) was inversely associated with inpatient complications (Supplementary Table 1).

4 | DISCUSSION

We found that obesity was not associated with the development of inpatient complications including myocardial infarction, renal failure requiring dialysis, secondary bacterial infection, stroke, or thromboembolic events during the early phase of the COVID-19 pandemic at a diverse urban safety-net hospital. Age and obstructive sleep apnea were associated with experiencing at least one inpatient complication. These findings provide additional data on complications associated with COVID-19 among persons with obesity in a setting with close monitoring and early administration of immunomodulatory therapy.

The results in this study differ from other studies showing that elevated BMI was associated with multiple complications. A multicenter analysis of the American Heart Association's COVID-19 Cardiovascular Disease registry observed associations between elevated BMI and increased risks of VTE and initiation of renal replacement therapy.¹⁶ Other studies found that individuals with obesity were more likely to require invasive mechanical ventilation and develop acute kidney injuries while hospitalized.^{17,18} It is possible that BMC's early implementation of a protocol including the use of immunomodulators improved outcomes and limited the development of COVID-19-related complications in this cohort. Notably, guidelines now suggest the use of tocilizumab for severe COVID-19 with evidence of systemic inflammation.¹⁹

In the current study, patients with obesity were significantly younger than patients without obesity (Table 1). A study in Italy of COVID-19 related deaths showed that obesity was associated with shock and acute renal failure.²⁰ However, the cohort evaluated in Italy was nearly 20 years older on average than the patient population evaluated in the current study. As prior work has previously shown that older age is associated with severe and critical COVID-19, it is possible that younger age served as a protective factor against developing inpatient complications in patients with obesity in the current study.²¹ Further, patient demographics differed substantially from the current study which may contribute to discrepancies across studies; patients in the current study less often identified as White (7.8% vs. 32.8%) and more often identified as Black (43.9% vs. 24.3%) and Latino or Hispanic (38.5% vs. 29.5%). According to the most recent Centers for Disease Control and Prevention data, Latino persons are 1.5 times more likely to develop COVID-19 and 2.3 times more likely to die from COVID-19. Black/African American persons are 1.1 times more likely to develop COVID-19 and 2.5 times more likely to die from COVID-19 than White persons.¹⁰ The diverse cohort seen at BMC significantly encompasses the racial and ethnic groups disproportionately affected by the COVID-19 pandemic.

The interaction between COVID-19, obesity, and race is complex and requires multimodal solutions to reduce disparities in

TABLE 1 Patient demographics, comorbidities, and hospital course

Covariate	Overall <i>n</i> = 374	BMI <30 kg/m ² <i>n</i> = 173 (46.3%)	BMI ≥30 kg/m ² <i>n</i> = 201 (53.7%)	<i>p</i> value
Demographics (<i>n</i> , %)				
Age, years (median, IQR)	57 (45–68)	62 (52–71)	52 (41–62)	<0.001
≤49	126 (33.7)	38 (22.0)	88 (43.8)	
50–64	127 (34.0)	58 (33.5)	69 (34.3)	
≥65	121 (32.4)	77 (44.5)	44 (21.9)	
Male sex	216 (57.8)	116 (67.1)	100 (49.8)	0.001
Race				0.018
Asian	6 (1.6)	5 (2.9)	1 (0.5)	
Black or African American	164 (43.9)	77 (44.5)	87 (43.3)	
Latino or Hispanic	144 (38.5)	57 (32.9)	87 (43.3)	
White	29 (7.8)	20 (11.6)	9 (4.5)	
Unknown	31 (8.3)	14 (8.1)	17 (8.5)	
Comorbidities				
Cardiac disease ^a	81 (21.7)	41 (23.7)	40 (19.9)	0.445
Hypertension	235 (62.8)	104 (60.1)	131 (65.2)	0.367
Diabetes	157 (42.0)	71 (41.0)	86 (42.8)	0.813
Chronic kidney disease ^b	69 (18.4)	30 (17.3)	39 (19.4)	0.705
Chronic pulmonary disease ^c	75 (20.1)	26 (15.0)	49 (24.4)	0.034
Obstructive sleep apnea	41 (11.0)	4 (2.3)	37 (18.4)	<0.001
Malignancy	30 (8.0)	17 (9.8)	13 (6.5)	0.317
Sickle cell disease	3 (0.8)	1 (0.6)	2 (1.0)	1.000
Cirrhosis	5 (1.3)	1 (0.6)	4 (2.0)	0.463
Human immunodeficiency virus	14 (3.7)	4 (2.3)	10 (5.0)	0.280
Experiencing homelessness	35 (9.4)	22 (12.7)	13 (6.5)	0.116
Baseline labs (median, IQR)				
CRP (mg/L)	80.1 (36.7, 143.2)	91.8 (36.2, 164.9)	73.4 (37.9, 121.6)	0.123
Ferritin (ng/ml)	587.0 (287.5, 1361.0)	616.5 (308.8, 1661.8)	580.0 (277.0, 1179.0)	0.372
LDH (U/L)	359.0 (294.8, 473.3)	346.0 (275.3, 456.8)	379.0 (311.5, 531.3)	0.142
WBC (1000 cells/μL)	6.6 (5.2, 9.1)	6.6 (5.0, 9.9)	6.7 (5.5, 8.5)	0.798
Supportive measures				
SpO ₂ /FiO ₂ (median, IQR)	452.4 (432.1, 466.7)	457.1 (433.3, 466.7)	452.4 (428.6, 461.9)	0.058
Immunomodulatory therapy	139 (37.2)	51 (29.5)	88 (43.8)	0.006
Hospital course				
ICU admission	105 (28.1)	41 (23.7)	64 (31.8)	0.103
Intubation	74 (19.8)	25 (14.5)	49 (24.4)	0.023
In-hospital death	33 (8.8)	17 (9.8)	16 (8.0)	0.652
Readmission ^d	19 (5.1)	10 (5.8)	9 (4.5)	0.897

Abbreviations: BMI, body mass index; CRP, C reactive protein; ICU, intensive care unit; IQR, interquartile range; LDH, lactate dehydrogenase; SpO₂/FiO₂, ratio of oxygen saturation to fraction of inspired oxygen; WBC, white blood cells.

^aCardiac disease defined as any history of coronary artery disease, congenital heart disease, or heart failure with preserved or reduced ejection fraction.

^bChronic kidney disease defined as stage III or higher, or on dialysis.

^cChronic pulmonary disease defined as chronic obstructive pulmonary disease or restrictive lung disease.

^dPrior to end of study data collection for any cause (October 2020).

TABLE 2 Inpatient complications

Inpatient complications	Overall <i>n</i> = 374	BMI <30 kg/m ² <i>n</i> = 173, (46.3%)	BMI ≥30 kg/m ² <i>n</i> = 201, (53.7%)	<i>p</i> value
General				
Myocardial infarction	12 (3.2)	9 (5.2)	3 (1.5)	0.083
Renal failure requiring dialysis	12 (3.2)	5 (2.9)	7 (3.5)	0.976
Stroke	1 (0.3)	0 (0.0)	1 (0.5)	1.000
Acute hepatocellular hepatitis	6 (1.6)	2 (1.2)	4 (2.0)	0.527
Infectious				
Bacteremia	17 (4.5)	8 (4.6)	9 (4.5)	1.000
Wound infection	3 (0.8)	2 (1.2)	1 (0.5)	0.896
Secondary bacterial infection	166 (44.4)	75 (43.4)	91 (45.3)	0.788
Thromboembolic				
Pulmonary embolism	10 (2.7)	6 (3.5)	4 (2.0)	0.574
Deep vein thrombosis	6 (1.6)	5 (2.9)	1 (0.5)	0.155

Abbreviation: BMI, body mass index.

TABLE 3 Multivariable analysis of hospital complications among patients with COVID-19

Covariate	aOR	95% CI	<i>p</i> value
Obesity ^a	1.19	0.73–1.93	0.488
Age	1.02	1.01–1.04	0.010
Male sex	1.53	0.98–2.42	0.066
Race/ethnicity			
Asian	2.13	0.30–20.13	0.466
Black	0.63	0.27–1.48	0.294
Latino or Hispanic	1.09	0.44–2.63	0.856
Unknown	0.77	0.25–2.27	0.630
Cardiac disease ^b	0.64	0.34–1.17	0.145
Diabetes	0.67	0.42–1.08	0.100
Chronic kidney disease ^c	1.22	0.65–2.27	0.538
Chronic pulmonary disease ^d	1.76	1.00–3.11	0.050
Obstructive sleep apnea	2.25	1.08–4.85	0.034
SpO ₂ /FiO ₂	0.95	0.92–0.98	0.002

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; SpO₂/FiO₂, ratio of oxygen saturation to fraction of inspired oxygen.

^aObesity defined as body mass index ≥30 kg/m².

^bCardiac disease defined as any history of coronary artery disease, congenital heart disease, or heart failure with preserved or reduced ejection fraction.

^cChronic kidney disease defined as stage III or higher, or on dialysis.

^dChronic pulmonary disease defined as chronic obstructive pulmonary disease or restrictive lung disease.

outcomes. For instance, weight management clinics are increasingly incorporating telemedicine models to improve access to care during the COVID-19 pandemic.²² However, access to telehealth

solutions remains limited in underserved communities, and these models do not address acute inpatient management.^{23,24} Conversely, the clinical factors identified in the current study may guide clinical decision-making at the bedside by informing patient-specific risk assessment for a set of inpatient complications in COVID-19.

Increased age and obstructive sleep apnea were independently associated with having at least one of the listed inpatient complications in the current study. In contrast, higher SpO₂/FiO₂ on admission was negatively associated with having at least one inpatient complication. Secondary bacterial infection was observed in 44.4% of patients in the current study, a much higher fraction than seen in similar studies.²⁵ This is likely reflective of empiric diagnosis and treatment of secondary bacterial pneumonia for patients in early stages of the pandemic.

A previous study of COVID-19 patients at the same institution as the current study found inflammatory markers were lower in patients with obesity and that more inflammation early in hospital course did not appear to mediate worse clinical outcomes; however, obesity was associated with increased rates of ICU admission and death.²⁵ In contrast, patients with obesity in the current study had similar baseline C-reactive protein, lactate dehydrogenase, and ferritin levels and similar ICU admission and mortality rates. These results suggest a reduced level of immune dysregulation present in members of the current cohort with obesity, potentially due to patients with obesity presenting earlier in their clinical course of COVID-19.

There were limitations to this study, including the use of data from early in the COVID-19 pandemic and retrospective study design. The use of a single site may reduce the study's generalizability, but the study's diverse cohort mitigates this. The study was not powered to detect differences in obesity rates or primary outcomes between races and ethnicities studied. However, we provide

useful information using a racially and ethnically diverse patient population. In addition, management protocols—including indications for immunomodulators, ICU admission, and intubation—changed throughout the study period due to the novelty of COVID-19 and may have introduced variability in outcomes. Further, there were limited reported complications, except for bacterial pneumonia. Lastly, this analysis did not incorporate social determinants of health such as income as almost 75% of patients at BMC come from underserved populations who rely on government payers such as Medicare and Medicaid.²⁶ Despite these limitations, these findings offer a novel characterization of obesity in COVID-19 that may provide insights on the natural history of COVID-19 and on the importance of early management and intervention especially among persons with obesity.

5 | CONCLUSIONS

Patients with obesity and COVID-19 in a racially and ethnically diverse cohort did not experience increased rates of inpatient complications. Rather, increased age and obstructive sleep apnea were associated with at least one inpatient complication. Future studies should further explore these findings in larger cohorts during the era of improved treatment options for COVID-19.

AUTHOR CONTRIBUTIONS

Tyler J. Ryan, Annie S. Heyman, Angela McLaughlin, and Sabrina A. Assoumou conceived and designed the study. Elizabeth N. Mulvey, Tyler J. Ryan, Annie S. Heyman, Angela McLaughlin, Sabrina A. Assoumou, and Ivania M. Rizo analyzed and interpreted the study data. Tyler J. Ryan, Annie S. Heyman, Angela McLaughlin, Sabrina A. Assoumou, and Elizabeth N. Mulvey drafted the manuscript. Elizabeth N. Mulvey and Sabrina A. Assoumou provided statistical expertise, and Sabrina A. Assoumou obtained funding for the study. All authors were involved in writing the paper and had final approval of the submitted and published versions.

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CONFLICT OF INTEREST

The authors declared no conflict of interest.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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