# Obesity and the Risk of Intubation or Death in Patients With Coronavirus Disease 2019

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**Objectives:** To characterize the impact of obesity on disease severity in patients with coronavirus disease 2019.

**Design:** This was a retrospective cohort study designed to evaluate the association between body mass index and risk of severe disease in patients with coronavirus disease 2019. Data were abstracted from the electronic health record. The primary endpoint was a composite of intubation or death.

**Setting:** Two hospitals in Massachusetts (one quaternary referral center and one affiliated community hospital).

**Patients:** Consecutive patients hospitalized with confirmed coronavirus disease 2019 admitted between March 13, 2020, and April 3, 2020.

**Interventions:** None.

**Measurements and Main Results:** A total of 305 patients were included in this study. We stratified patients by body mass index category: $< 25\,kg/m^2$ (54 patients, 18%), $\geq 25\,kg/m^2$ to $< 30\,kg/m^2$ (124 patients, 41%), $\geq 30\,kg/m^2$ to $< 35\,kg/m^2$ (58 patients, 19%), and $\geq 35\,kg/m^2$ (69 patients, 23%). In total, 128 patients (42%) had a primary endpoint (119 patients [39%] were intubated and nine died [3%] without intubation). Sixty-five patients (51%) with body mass index greater than or equal to $30\,kg/m^2$ were intubated or died. Adjusted Cox models demonstrated that body mass index greater than or equal to $30\,kg/m^2$ was associated with a 2.3-fold increased risk of intubation or death (95% CI, 1.2–4.3) compared with individuals with body mass index less than $25\,kg/m^2$. Diabetes was also independently associated with risk of intubation or death (hazard ratio, 1.8; 95% CI, 1.2–2.7). Fifty-six out of 127 patients (44%) with body mass index greater than or equal to $30\,kg/m^2$ had diabetes, and the combination of both diabetes and body mass index greater than or equal to $30\,kg/m^2$ was associated with a 4.5-fold increased risk of intubation or death (95% CI, 2.0–10.2) compared with patients without diabetes and body mass index less than $25\,kg/m^2$.

**Conclusions:** Among consecutive patients hospitalized with coronavirus disease 2019, obesity was an independent risk factor for intubation or death. (*Crit Care Med* 2020; XX:00–00)

**Key Words:** coronavirus disease 2019; intubation; obesity; respiratory failure

The identification of risk factors for disease severity in patients with coronavirus disease 2019 (COVID-19) is paramount for both risk mitigation and treatment strategies. Although the Centers for Disease Control and Prevention has identified body mass index (BMI) greater than $40\,kg/m^2$ as an independent risk factor for severe illness, there is limited data supporting this association (1, 2). Therefore, we characterized the relationship between BMI and severe respiratory disease requiring intubation and mechanical ventilation or death in a multicenter cohort of consecutively hospitalized patients with confirmed COVID-19.

## MATERIALS AND METHODS

This retrospective cohort study included 305 consecutively hospitalized patients with confirmed COVID-19 at two hospitals in Massachusetts (one quaternary referral center and one affiliated community hospital) admitted between March 13, 2020, and April 3, 2020. Data elements were abstracted from the electronic health record (EHR) by trained study personnel following a standardized protocol. BMI was calculated based on height and weight obtained from the EHR. Height and weight were abstracted from the flowsheet values entered by healthcare workers during admission. Heights were obtained through measurement (either from prior ambulatory visits or measurement on hospital arrival) and self-report. Weights

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were predominantly measured using bed scales. Study data were collected and managed using Research Electronic Data Capture (REDCap) electronic data capture tools (3). This study was approved by the Partners Healthcare Institutional Review Board.

The primary endpoint was the time from hospital presentation to a composite of intubation or death (4). For patients who subsequently died after intubation, the primary endpoint was classified as time to intubation (4). The population was stratified by BMI category: < 25 kg/m$^2$, ≥ 25 to < 30 kg/m$^2$, ≥ 30 kg/m$^2$ to < 35 kg/m$^2$, and ≥ 35 kg/m$^2$. Baseline characteristics were evaluated for trend across BMI strata. Linear regression (parametric), and the Jonckheere-Terpstra test (nonparametric) were used for continuous variables. Trends for categorical variables were assessed using the Cochran-Armitage trend test (binary) and the Cochran-Mantel-Haenszel test (more than two levels). Kaplan-Meier estimates and Cox proportional hazard models were used to evaluate risk of the primary endpoint according to BMI category. Results are presented as hazard ratios (HRs) with 95% CIs. Models were adjusted for age, gender, race/ethnicity, hypertension, diabetes, coronary artery disease, asthma/chronic obstructive pulmonary disease, and prior use of angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker. Effect modification (by age, gender, race/ethnicity, and diabetes) was evaluated using interaction terms in the Cox models. The proportional hazards assumptions were met. Statistical analysis was performed using SAS software (version 9.4; SAS Institute, Cary, NC).

## RESULTS

Of the 305 patients in our cohort, mean age was 60 years (SD, 18 yr) and slightly fewer than half of the cohort (42%) were women. Racial/ethnic breakdown included 126 (41%) White, 30 (10%) Black, 112 (37%) Hispanic/Latino, 11 (4%) Asian, 6 (2%) other, and 20 (6%) patients with unreported race/ethnicity. Median BMI was 28.8 (interquartile range [IQR], 25.8–33.9) and the distribution by BMI category included as follows: 54 (18%) < 25 kg/m$^2$, 124 (40%) ≥ 25 to < 30 kg/m$^2$, 58 (19%) ≥ 30 kg/m$^2$ to < 35 kg/m$^2$, and 69 (23%) ≥ 35 kg/m$^2$. Baseline demographics, comorbidities, medications, initial vital signs, and laboratory data are presented by BMI strata in **Table 1**. Patients with a higher BMI were younger ($p$ trend = 0.0001) and more likely to have diabetes ($p$ trend = 0.02). Otherwise, baseline demographics, comorbidities, and medication use did not differ between BMI categories.

The average time from symptom onset to hospital presentation was 7.3 days (SD, 4.6 d) and there was no difference across BMI category. On presentation, patients with higher BMI were more likely to report symptoms of dyspnea and require supplemental oxygen ($p$ trend = 0.008 and 0.01, respectively). The median respiratory rate on presentation was elevated at 22 breaths per minute (IQR, 18–28 breaths/min) and increased with higher BMI category ($p$ trend = 0.01). Baseline laboratory values were notable for elevations in markers of inflammation (C-reactive protein, ferritin, D-dimer, and procalcitonin) that were not significantly different across BMI strata.

Over median follow-up of 9 days (IQR, 6–14 d), 128 patients (42%) had a primary endpoint (119 were intubated, nine died without intubation). The proportion of patients who met the primary endpoint by BMI category were: 30% for BMI < 25 kg/m$^2$, 38% for BMI ≥ 25 kg/m$^2$ to < 30 kg/m$^2$, 52% for BMI ≥ 30 kg/m$^2$ to < 35 kg/m$^2$, and 51% for BMI ≥ 35 kg/m$^2$ ($p$ trend = 0.006). Kaplan-Meier curves showing event-free survival over time according to BMI strata are shown in **Figure 1*A***. Cox models showed that BMI greater than or equal to 30 kg/m$^2$ was associated with a significantly increased risk of intubation or death when compared with BMI ≥ 30 kg/m$^2$ to < 35 kg/m$^2$ (HR, 2.1; 95% CI, 1.2–3.9; $p$ = 0.02) and BMI ≥ 35 kg/m$^2$ (HR, 2.0; 95% CI, 1.1–3.6; $p$ = 0.02). In contrast, BMI greater than or equal to 25 kg/m$^2$ to less than 30 kg/m$^2$ was not (HR, 1.4; 95% CI, 0.8–2.6; $p$ = 0.2). Multivariable adjusted Cox models showed that BMI greater than or equal to 30 kg/m$^2$ remained independently associated with an increased risk of intubation or death when compared with BMI less than 25 kg/m$^2$: BMI ≥ 30 kg/m$^2$ to < 35 kg/m$^2$ (HR, 2.3; 95% CI, 1.2–4.3; $p$ = 0.01) and BMI ≥ 35 kg/m$^2$ (HR, 2.3; 95% CI, 1.2–4.3; $p$ = 0.008) (**Fig. 1*B***). Similar to the unadjusted model, BMI greater than or equal to 25 to less than 30 kg/m$^2$ was not associated with a significantly increased risk of intubation or death (HR, 1.6; 0.9–2.9; $p$ = 0.1). Diabetes was also independently associated with risk for intubation or death (HR, 1.8; 1.2–2.7; $p$ = 0.003). A total of 56 out of 127 patients (44%) with BMI greater than or equal to 30 kg/m$^2$ had diabetes. Thirty-five out of 56 patients (63%) with both diabetes and BMI greater than or equal to 30 kg/m$^2$ were intubated or died. After multivariable adjustment, the combination of diabetes and BMI greater than or equal to 30 kg/m$^2$ was associated with a 4.5-fold increased risk (95% CI, 2.0–10.2) of the primary endpoint compared with those with BMI less than 25 kg/m$^2$ and no diabetes ($p$ = 0.0003). Interaction testing for BMI with age, gender, race/ethnicity, and diabetes was not significant.

For the 119 patients who required intubation, median time to intubation was 12 hours (IQR, 2–48 hr) and there was no difference by BMI category ($p$ = 0.43).

At time of censoring, 33 patients (11%) had died, 190 (62%) were discharged from the hospital, and 82 (27%) were still hospitalized. These rates did not differ by BMI category.

In a sensitivity analysis looking specifically at risk of intubation, BMI greater than or equal to 30 kg/m$^2$ was independently associated with increased risk of intubation. BMI ≥ 30 kg/m$^2$ to < 35 kg/m$^2$ (HR, 2.2; 95% CI, 1.1–4.3; $p$ = 0.02) and BMI ≥ 35 kg/m$^2$ (HR, 2.3; 95% CI, 1.2–4.5; $p$ = 0.01). Similarly, the combination of diabetes and obesity was independently associated with increased risk of intubation compared with those without either risk factor (HR, 4.9; 95% CI, 2.0–12.2; $p$ = 0.0006).

## DISCUSSION

In this cohort of consecutively hospitalized patients with confirmed COVID-19, we demonstrate that obesity (BMI ≥ 30 kg/m$^2$) is a strong, independent, and clinically relevant risk factor

**TABLE 1. Baseline Characteristics Stratified by Body Mass Index Category**

| BMI Categories | All ($n = 305$) | BMI < 25 ($n = 54$) | BMI ≥ 25 to < 30 ($n = 124$) | BMI ≥ 30 to < 35 ($n = 58$) | BMI ≥ 35 ($n = 69$) | *p* Trend |
|---|---|---|---|---|---|---|
| Baseline demographics | | | | | | |
| Age, yr, mean (SD) | 60 (18) | 68 (19) | 61 (17) | 58 (16) | 56 (17) | 0.0001 |
| Female, *n* (%) | 127 (42) | 19 (35) | 47 (38) | 28 (48) | 33 (48) | 0.07 |
| Race/ethnicity, *n* (%) | | | | | | 0.08 |
| Caucasian | 126 (41) | 27 (50) | 51 (41) | 20 (35) | 28 (41) | |
| Black | 30 (10) | 4 (7) | 16 (13) | 6 (10) | 4 (6) | |
| Hispanic | 112 (37) | 17 (31) | 37 (30) | 28 (48) | 30 (43) | |
| Asian | 11 (4) | 1 (2) | 9 (7) | 0 | 1 (1) | |
| Other | 6 (2) | 2 (4) | 1 (1) | 1 (2) | 2 (3) | |
| Unknown | 20 (6) | 3 (6) | 10 (8) | 3 (5) | 4 (6) | |
| Baseline comorbidities | | | | | | |
| Hypertension, *n* (%) | 158 (52) | 35 (65) | 52 (42) | 32 (55) | 39 (57) | 0.87 |
| Diabetes, *n* (%) | 106 (35) | 18 (33) | 32 (26) | 25 (43) | 31 (45) | 0.02 |
| Coronary artery disease, *n* (%) | 41 (13) | 11 (20) | 17 (14) | 6 (10) | 7 (10) | 0.10 |
| Heart failure, *n* (%) | 24 (8) | 7 (13) | 6 (5) | 7 (12) | 4 (6) | 0.51 |
| Asthma/chronic obstructive pulmonary disease, *n* (%) | 55 (18) | 11 (20) | 21 (17) | 8 (14) | 15 (22) | 0.84 |
| Chronic kidney disease (Cr > 3 mg/dL), *n* (%) | 11 (4) | 3 (6) | 4 (3) | 3 (5) | 1 (1) | 0.35 |
| Charlson Comorbidity Index, median (IQR) | 1 (0–2) | 1 (0–4) | 1 (0–2) | 1 (0–2) | 1 (0–2) | 0.2 |
| Baseline medications, *n* (%) | | | | | | |
| Angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker | 85 (28) | 17 (31) | 29 (23) | 16 (28) | 23 (33) | 0.50 |
| Statins | 134 (44) | 25 (46) | 56 (45) | 21 (36) | 32 (46) | 0.79 |
| Aspirin | 81 (27) | 15 (28) | 29 (23) | 15 (26) | 22 (32) | 0.43 |
| Characteristics on hospital presentation | | | | | | |
| Dyspnea on presentation, *n* (%) ($n = 300$) | 212 (71) | 29 (55) | 86 (71) | 43 (75) | 54 (78) | 0.008 |
| Respiratory rate ($n = 303$), median (IQR) | 22 (18–28) | 20 (18–26) | 22 (18–28) | 22 (20–28) | 23 (20–28) | 0.01 |
| $Spo_2$, median (IQR) | 96 (93–98) | 96 (93–98) | 96 (94–98) | 95 (93–98) | 95 (93–97) | 0.2 |
| Oxygen requirement, *n* (%) ($n = 304$) | 80 (26) | 10 (19) | 27 (22) | 19 (33) | 24 (35) | 0.01 |
| Initial laboratory data | | | | | | |
| Cr (mg/dL), median (IQR) | 0.95 (0.80–1.16) | 0.96 (0.80–1.28) | 0.97 (0.82–1.20) | 0.90 (0.77–1.08) | 0.94 (0.80–1.11) | 0.2 |
| Ferritin (μg/L) ($n = 298$), median (IQR) | 592 (274–1,100) | 493 (204–1,162) | 626 (316–1,261) | 699 (395–1,136) | 428 (225–846) | 0.7 |
| Absolute lymphocyte count (K), median (IQR) | 0.9 (0.6–1.3) | 0.7 (0.6–1.2) | 0.9 (0.6–1.3) | 1.0 (0.7–1.3) | 1.0 (0.7–1.3) | 0.03 |
| D-dimer (ng/mL) ($n = 285$), median (IQR) | 930 (613–1,515) | 820 (550–1,283) | 993 (645–1,693) | 916 (613–1,253) | 838 (548–1,298) | 0.6 |
| C-reactive protein (mg/L) ($n = 291$), median (IQR) | 75.1 (35.9–148.0) | 58.2 (20.3–145.9) | 76.0 (42.4–167.5) | 96.8 (58.1–148.2) | 74.7 (33.2–145.0) | 0.2 |
| Procalcitonin (ng/mL) ($n = 276$), median (IQR) | 0.16 (0.09–0.30) | 0.18 (0.12–0.32) | 0.14 (0.09–0.24) | 0.18 (0.10–0.37) | 0.13 (0.08–0.31) | 0.6 |
| P:F ratio[a] ($n = 119$), mean (SD) | 202 (92) | 226 (111) | 224 (91) | 192 (100) | 170 (70) | 0.007 |
| P:F ratio[a] < 200, *n* (%) ($n = 119$) | 64 (54) | 4 (29) | 17 (39) | 19 (68) | 24 (73) | 0.0003 |
| Initial positive end-expiratory pressure[b] (cm $H_2O$), median (IQR) | 10 (8–12) | 10 (8–12) | 10 (8–10) | 10 (8–11) | 12 (10–14) | 0.03 |

BMI = body mass index, Cr = creatinine, IQR = interquartile range.

[a]Post-intubation.

[b]At time of first arterial blood gas.

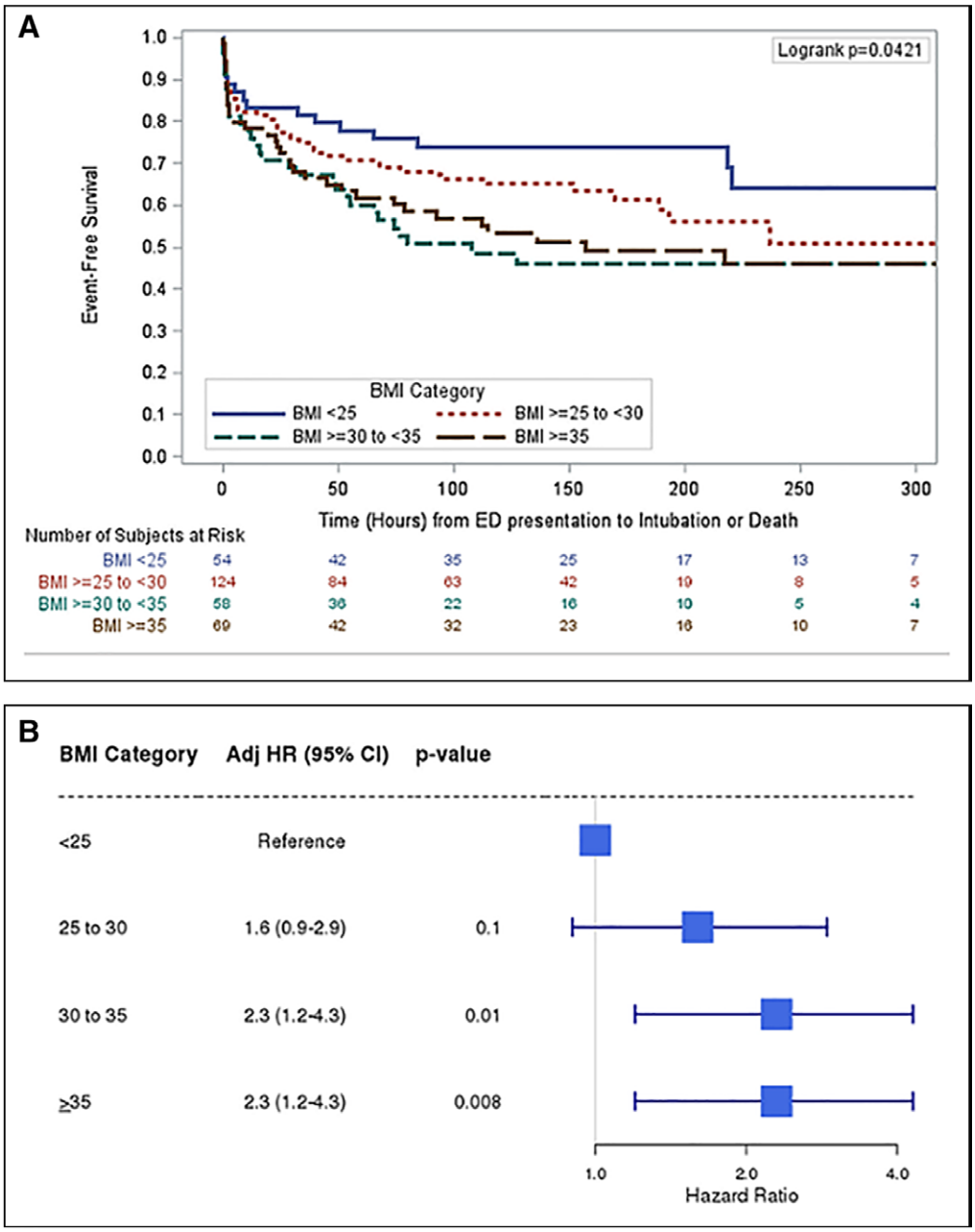


**Figure 1.** Risk of intubation or death according to body mass index (BMI) category. **A**, Kaplan-Meier plot of event-free survival according to BMI category. Primary endpoint: composite of intubation or death. **B**, Forest plot of multivariable-adjusted hazard ratios (HRs) and 95% CIs according to BMI category. Primary endpoint: composite of intubation or death. Model adjusted for age, gender, race/ethnicity, diabetes, hypertension, coronary artery disease, asthma/chronic obstructive pulmonary disease, and prior use of angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker. ED = emergency department.

for severe illness leading to intubation or death. The data show that patients with higher BMI have more respiratory distress on initial hospital presentation (increased dyspnea, need for supplemental oxygen, and higher respiratory rate) and higher rates of intubation. These data support the concept that obesity is associated with a greater degree of respiratory compromise in patients with COVID-19.

Our findings are consistent with and expand upon two prior studies evaluating the impact of BMI in patients with COVID-19. A single-center study from France reported that BMI greater than or equal to 35 kg/m$^2$ was independently associated with the need for mechanical ventilation in 124 patients already in the ICU (5). An additional single-center study from the United States demonstrated that BMI greater than or equal to 30 kg/m$^2$ was associated with an increased risk for hospitalization and critical care (6). However, because comorbidities were not reported or adjusted for, it remained unclear whether BMI greater than or equal to 30 kg/m$^2$ was an independent risk factor for illness severity or simply a marker of other cardiometabolic risk factors (i.e., diabetes, hypertension) known to be associated with poor outcomes in patients with COVID-19 (1, 7). Our study expands upon the limited existing literature by providing support for BMI greater than or equal to 30 kg/m$^2$ as an independent risk factor for severe respiratory illness in patients with COVID-19. In addition, our study demonstrates that the combination of obesity and diabetes independently and synergistically portends an increased risk of severe disease leading to intubation or death.

The mechanism of obesity as a risk factor for intubation and severe COVID-19 has yet to be elucidated; however, obesity and metabolic syndrome have been associated with immune dysfunction and increased risk of pneumonia (7–9). Proposed mechanisms for obesity contributing to severe respiratory illness in patients with COVID-19 include impaired respiratory mechanics, restrictive lung physiology caused by excess body weight, and poor pulmonary reserve (7, 9, 10). In addition, other possible mechanisms include a dysregulated immune response on the background of chronic inflammation and vascular endothelial dysfunction leading to increased thrombotic events (10).

Ultimately, the identification of risk factors for severe COVID-19 may help stratify high-risk patients and facilitate mitigation and treatment strategies. Given the high prevalence of obesity

in the general population, coupled with the association between obesity and other cardiometabolic risk factors (known to be associated with severe COVID-19), there have been calls for better characterization of the independent relationship between BMI and risk of severe COVID-19 (1, 2, 7). Our findings help to refine and confirm the independent association between BMI and increased risk for severe COVID-19.

Limitations of our study include a small sample size from a single geographic region and lack of long term follow-up. Due to the small number of patients with BMI greater than or equal to 40, we were not able to independently analyze higher BMI categories (i.e., $\geq 35\,kg/m^2$ to $< 40\,kg/m^2$ and $\geq 40\,kg/m^2$). Additionally, although the value for height was a clinically recorded value that was used by the clinical team to guide therapy (i.e., calculate ideal body weight for tidal volume calculations), some of these values were based on self-report, which could impact accuracy of BMI calculations. The strengths of our study include in-depth phenotyping of a racially and ethnically diverse population from two different hospitals (one quaternary referral center and one community hospital).

## CONCLUSIONS

Among patients hospitalized with COVID-19, obesity (BMI $\geq 30\,kg/m^2$) was associated with an increased risk of intubation or death. This risk was independent of age and other comorbidities that have been associated with severe COVID-19. Further investigation is warranted to elucidate mechanisms and potential therapeutic approaches.

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