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MAYO CLINIC

ORIGINAL ARTICLE

Obesity is a Major Risk Factor for Hospitalization in Community-Managed COVID-19 Pneumonia

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Abstract

Objective: We aimed to investigate whether the stratification of outpatients with coronavirus disease 2019 (COVID-19) pneumonia by body mass index (BMI) can help predict hospitalization and other severe outcomes.

Patients and Methods: We prospectively collected consecutive cases of community-managed COVID-19 pneumonia from March 1 to April 20, 2020, in the province of Bergamo and evaluated the association of overweight (25 kg/m^2 $\leq$ BMI $<$30 kg/m^2) and obesity ($\geq$30 kg/m^2) with time to hospitalization (primary end point), low-flow domiciliary oxygen need, noninvasive mechanical ventilation, intubation, and death due to COVID-19 (secondary end points) in this cohort. We analyzed the primary end point using multivariable Cox models.

Results: Of 338 patients included, 133 (39.4%) were overweight and 77 (22.8%) were obese. Age at diagnosis was younger in obese patients compared with those overweight or with normal weight ($P<.001$), whereas diabetes, dyslipidemia, and heart diseases were differently distributed among BMI categories. Azithromycin, hydroxychloroquine, and prednisolone use were similar between BMI categories ($P>.05$). Overall, 105 (31.1%) patients were hospitalized, and time to hospitalization was significantly shorter for obese vs over- or normal-weight patients ($P<.001$). In the final multivariable analysis, obese patients were more likely to require hospitalization than nonobese patients (hazard ratio, 5.83; 95% CI, 3.91 to 8.71). Results were similar in multiple sensitivity analyses. Low-flow domiciliary oxygen need, hospitalization with noninvasive mechanical ventilation, intubation, and death were significantly associated with obesity ($P<.001$).

Conclusion: In patients with community-managed COVID-19 pneumonia, obesity is associated with a higher hospitalization risk and overall worse outcomes than for nonobese patients.

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Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a novel coronavirus first detected in Wuhan, China, in December 2019 that spread all over the world in the following weeks.[1] Patients infected by SARS-CoV-2 develop coronavirus disease 2019 (COVID-19), characterized by a high rate of hospitalization, respiratory failure, and ultimately death.[2-7] Coexisting conditions, such as diabetes, hypertension, malignancy, chronic obstructive pulmonary disease, and older age, are risk factors for severe disease and poor outcome in hospitalized patients. Obesity has been shown to be highly prevalent in patients requiring hospital care or invasive mechanical ventilation[8-13] and to be associated with in-hospital mortality after adjustment for other comorbid conditions.[14]

In the most affected countries, the asymptomatic and noncritical patients with active infection were treated at home to avoid the collapse of the health systems. The Lombardy region in Italy and specifically the province of Bergamo has been severely affected by COVID-19, after the first case was detected in Alzano Lombardo on

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February 23.[15] The highest rates of infection and death in Italy were registered in this province, unfortunately making this area the ideal epidemiologic setting to study COVID-19.

We aimed to examine the association of increased body mass index (BMI; calculated as the weight in kilograms divided by the height in meters squared) with hospitalization and severe outcomes in a nonhospital setting of COVID-19 pneumonia. We collected all consecutive cases of community-managed COVID-19 pneumonia during the early weeks of the pandemic (March 1 to April 20, 2020) from a large cohort of residents in the province of Bergamo followed up by 35 primary care providers and evaluated the association of overweight and obesity with time to hospitalization (primary end point), domiciliary low-flow oxygen need, noninvasive mechanical ventilation (NIV), intubation, and death due to COVID-19 (secondary end points).

PATIENTS AND METHODS

Setting and Data Sources

We conducted a prospective observational cohort study in the province of Bergamo area, Italy. Study participants were recruited from the adult general population (aged ≥18 years) among approximately 40,000 residents followed up by 35 primary care providers (ie, up to 1500 patients for each general practitioner, ranging from 1000-1500) from March 1, 2020, to April 20, 2020. Follow-up continued until death or May 31, 2020. The electronic medical records of the recruited outpatients were accessed by the respective providers and data were manually abstracted. The availability of this comprehensive medical data, which systematically collect all clinical records of each individual in the province, allowed a detailed case ascertainment.

Case Ascertainment and Variables Assessed

Incident cases of COVID-19 pneumonia were collected during the study period, that is, the early phases of pandemic in Lombardy. All adults with at least 2 of the following 4 symptoms (temperature ≥37.5°C, cough, pleuritic chest pain, and dyspnea) with pneumonia documented using computed tomography (CT) between March 1, 2020, and April 20, 2020, were included in the study. Patients were tested using reverse transcriptase–polymerase chain reaction (RT-PCR) assay for SARS-CoV-2 when clinically indicated by the local health authority. Patients not fulfilling these criteria, including asymptomatic or low-symptomatic cases without pneumonia, even if positive for SARS-CoV-2 at RT-PCR, were excluded. Patients with acute respiratory distress syndrome[16] and/or requiring hospitalization and/or respiratory support at onset were not included. Patients with evidence of bacterial pneumonia (ie, clear imaging signs of bacterial pneumonia according to the radiologic report) were also excluded.

Patients were treated for COVID-19 infection according to medical judgment, following a shared protocol provided by the referral hospital Giovanni XXIII of Bergamo, which included hydroxychloroquine (HCQ), 200 mg, 12 hours apart for the first 2 doses, then 200 mg/day for 5 or more days; oral azithromycin, 500 mg/day, for 5 or more days; oral cefixime, 400 mg/day, for 5 or more days; oral prednisolone or equivalents, 5 to 25 mg/day, for 5 or more days; and subcutaneous enoxaparin, 4000 U/day, until mobilization or resolution of phlebitis. In general, patients started treatment with azithromycin with or without HCQ, and cefixime was added after 5 days if no improvement was seen, in case of macrolide allergy, or in addition to previous treatments in patients 65 years or older or with 1 or more comorbid condition. Prednisolone and enoxaparin were added according to clinical judgment.

General practitioners were allowed to prescribe domiciliary low-flow oxygen therapy to patients with oxygen saturation less than 93% at rest while breathing ambient air documented by pulse oximeter (<90% for patients affected by chronic obstructive pulmonary disease) or heart rate greater

than 22 beats/min. Data for patient demographic characteristics, baseline comorbid conditions, presenting symptoms, oxygen saturation while breathing ambient air at presentation, historical and current medication list, low-flow oxygen prescription by the general practitioners, inpatient hospitalization, invasive and noninvasive ventilator use data, and death were collected.

The study was conducted according to Strengthening the Reporting of Observational Studies in Epidemiology guidelines for cohort studies. This study was conducted in compliance with the Good Clinical Practice protocol and the Declaration of Helsinki principles and was approved by the local institutional review board.

BMI Assessment

The most recent patient weight and height during the 12 months preceding the index date (diagnosis of pneumonia) were collected, and BMI was calculated as described. Patients were stratified by BMI as normal weight (BMI <25 kg/m^2), overweight (25 kg/m^2 $\leq$ BMI <30 kg/m^2), and obese ($\geq$30 kg/m^2), according to the World Health Organization definitions.[17]

Study End Points

The primary end point was the time from the index date to hospitalization due to COVID-19 (time-to-event outcome). Secondary end points were time from the index date to death due to COVID-19 and the associations of BMI categories with hospitalization, domiciliary low-flow oxygen need, NIV, intubation, and death during the observation period.

Statistical Analyses

Categorical data were summarized as percentage, significant difference, or associations of BMI categories with secondary end points, or other clinical features were analyzed using χ^2 test or Fisher exact tests, when appropriate. Continuous variables were presented as mean $\pm$ SD or median and interquartile range, depending on normality demonstrated using the Kolmogorov-Smirnov test. Comparisons were performed using either Student t test for independent samples (2 tailed) or with analysis of variance comparisons with Bonferroni correction when the mean values of the 3 BMI categories were being compared.

Cox proportional hazard regression models were used to estimate the association between obesity and hospitalization (primary end point). Patients without a primary end point event had their data censored on May 31, 2020. An initial multivariable Cox regression model included as covariates demographic factors, comorbid conditions at diagnosis, and treatment for community-managed COVID-19 pneumonia. A Cox regression model including as covariates only those with significant P values at univariate analysis was performed and reported. The estimated distribution of hospitalization and death was performed using the Kaplan-Meier method and log-rank test. Multiple imputation was used to handle missing data, and model estimates and standard errors were calculated using Rubin's rules.[18]

All analyses were performed using JMP Pro package (SAS Institute Inc) and SAS System for Windows, version 9.4 (SAS Institute), and $P<.05$ was considered statistically significant for all analyses.

RESULTS

Clinical Presentation and Specific Treatments

Of the 341 consecutive patients, 3 were excluded because patients did not meet the study criteria (ie, evidence of bacterial pneumonia on CT). A total of 338 patients were included in the analysis. Distributions of BMI ranged from 17.0 to 41.4 kg/m^2 (Supplemental Figure 1, available online at http://www.mayoclinicproceedings.org); 133 (39.4%) patients were overweight and 77 (22.8%) patients were obese.

Baseline demographic and clinical features are described in Table 1. Age at diagnosis was younger in obese (BMI $\geq$30 kg/m^2) patients compared with overweight (25 kg/m^2 $\leq$ BMI <30 kg/m^2) and normal-weight (BMI <25 kg/m^2) patients ($P<.001$ in both cases by direct comparison), while

TABLE 1. Demographic Characteristics and Baseline Comorbid Conditions of Patients With Community-Managed COVID-19 Pneumonia by BMI[a]

Characteristic	All Patients (N=338)	Normal-Weight Patients (BMI <25 kg/m^2) (n=133)	Overweight Patients (25 kg/m^2 ≤BMI <30 kg/m^2) (n=128)	Obese Patients (BMI ≥30 kg/m^2) (n=77)	P[b]
Age at diagnosis (y), mean ± SD	65.7±13.1	66.5±14.9	67.4±11.6	61.3±12.1	.003
Male sex, % (no.)	59.4 (201)	45.9 (61)	67.2 (86)	70.1 (54)	<.001
Body weight (kg), mean ± SD	79.8±17.4	66.2±9.5	82.4±12.1	99.0±15.0	<.0001
Height (m), mean ± SD	1.8±0.09	1.7±0.09	1.7±0.09	1.7±0.10	.612
Ethnicity, White, % (no.)	91.4 (309)	90.2 (120)	89.8 (115)	96.1 (74)	.421
Smoking, current or former, % (no.)	26.9 (91)	28.7 (37)	31.3 (40)	18.12 (14)	.119
Pack/years, mean ± SD	18±6	20±7	17±6	16±4	.112
No comorbid conditions, % (no.)	11.0 (37)	14.3 (19)	8.6 (11)	9.1 (7)	.284
Diabetes, % (no.)	24.3 (82)	33.8 (45)	14.8 (19)	23.4 (18)	.002
Blood hypertension, % (no.)	45.23 (153)	48.9 (65)	39.8 (51)	48.1 (37)	.293
Angiotensin-converting enzyme inhibitors, % (no.)	14.2 (48)	17.3 (23)	10.9 (14)	14.3 (11)	.339
Angiotensin II receptor blockers, % (no.)	9.8 (33)	9.8 (13)	10.2 (13)	9.1 (7)	.9670
Dyslipidemia, % (no.)	27.8 (94)	18.1 (24)	37.5 (48)	28.6 (22)	.002
Heart diseases, % (no.)	24.9 (83)	31.6 (42)	14.8 (19)	28.6 (22)	.005
Cancer, % (no.)	6.9 (23)	7.7 (10)	6.3 (8)	6.5 (5)	.891
Chronic kidney disease stage ≥3,[c] % (no.)	2.7 (9)	3.0 (4)	3.9 (5)	0 (0)	.224
Asthma, % (no.)	3.6 (12)	6.0 (8)	1.6 (2)	2.6 (2)	.133
Chronic obstructive pulmonary disease , % (no.)	10.6 (36)	12.8 (17)	12.5 (16)	3.9 (3)	.091

[a]BMI, body mass index; COVID-19, coronavirus disease 2019; heart disease, chronic heart failure, myocardial infarction, atrial fibrillation.
[b]One-way analysis of variance: cut-off for *P* value interpretation after Bonferroni correction = .017.
[c]Chronic kidney disease stage 3 corresponds to estimated glomerular filtration rate less than 60 mL/min.

the prevalence of male sex increased with higher BMI (*P*<.001 for both obese and overweight vs normal-weight patients, by direct comparisons). Diabetes, dyslipidemia, and heart disease were differently distributed among the BMI categories. By direct comparison, diabetes was more frequent in normal-weight compared with overweight patients, while dyslipidemia was more frequent in overweight compared with normal-weight patients (*P*<.001 for both). Heart diseases were higher in obese compared with overweight patients and in normal-weight compared with overweight patients (*P*=.001 and *P*=.02, respectively).

The proportions of patients reporting headache, syncope/presyncope, dyspnea at rest, and oxygen desaturation (<93% while breathing ambient air) progressively increased with the increasing of BMI categories, while rhinorrhea/nasal obstruction progressively decreased (Table 2). Overall, approximately 42.0% (142/338) of patients underwent nasal swab testing for RT-PCT confirmation, and all of them had positive results.

The cumulative frequency of each drug used during the observation period for the treatment of COVID-19 pneumonia is reported in Table 2. Virtually all patients used azithromycin, more than half used HCQ, and approximately one-third used a low-medium dose of oral prednisolone or equivalents. Overall, no difference was observed among BMI categories, with the exception of paracetamol.

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TABLE 2. Clinical Features at Presentation and Specific Treatments of Patients With Community-Managed COVID-19 Pneumonia by BMI[a,b]

Characteristic	All Patients (N=338)	Normal-Weight Patients (BMI <25 kg/m^2) (n=133)	Overweight Patients (25 kg/m^2 ≤BMI <30 kg/m^2) (n=128)	Obese Patients (BMI ≥30 kg/m^2) (n=77)	P[c]
Clinical presenting features					
Temperature >37.5°C, % (no.)	98.5 (333)	98.5 (131)	100.0 (128)	96.1 (74)	.082
Fatigue, % (no.)	85.5 (289)	82.0 (109)	86.7 (111)	89.6 (69)	.280
Myalgia, % (no.)	58.9 (199)	54.9 (73)	58.6 (75)	66.2 (51)	.277
Arthralgia, % (no.)	70.1 (237)	61.7 (82)	72.7 (93)	80.5 (62)	.012
Anorexia, % (no.)	53.0 (179)	51.1 (68)	54.7 (70)	53.3 (41)	.850
Headache, % (no.)	29.3 (99)	23.3 (31)	21.9 (28)	52.0 (40)	<.001
Conjunctivitis, % (no.)	24.9 (84)	22.6 (30)	23.4 (30)	31.2 (24)	.355
Rhinorrhea/nasal obstruction, % (no.)	40.2 (136)	51.1 (68)	35.9 (46)	28.6 (22)	.003
Hyposmia, % (no.)	64.8 (219)	60.9 (81)	70.3 (90)	62.3 (48)	.235
Dysgeusia, % (no.)	43.8 (148)	38.4 (51)	45.3 (58)	50.7 (39)	.206
Gastrointestinal symptoms, % (no.)	51.2 (173)	30.8 (41)	65.6 (84)	62.3 (48)	<.001
Syncope/presyncope, % (no.)	27.2 (92)	15.8 (21)	26.6 (34)	48.1 (37)	<.001
Dry cough, % (no.)	85.2 (288)	82.0 (109)	87.5 (112)	87.0 (67)	.414
Dyspnea at rest, % (no.)	75.4 (255)	61.7 (82)	77.3 (99)	96.1 (74)	<.001
Dyspnea on exertion, % (no.)	94.4 (319)	93.2 (124)	92.2 (118)	100.0 (77)	.023
Oxygen saturation <93% in ambient air, % (no.)	79.6 (269)	68.4 (91)	82.8 (106)	93.5 (72)	<.001
Performed swab test, % (no.)	42.0 (142)	32.3 (43)	32.0 (41)	75.3 (58)	<.001
Positive swab test, % (no.)	100.0 (142)	100.0 (43/43)	100.0 (41/41)	100.0 (58/58)	>.99
Specific treatments					
Acetaminophen, % (no.)	95.6 (323)	91.7 (122)	99.2 (127)	96.1 (74)	.013
Nonsteroidal anti-inflammatory drug, % (no.)	50.9 (172)	50.4 (67)	51.6 (66)	50.7 (39)	.981
HCQ, % (no.)	54.7 (185)	60.9 (81)	50.0 (64)	52.0 (40)	.179
Azithromycin, % (no.)	98.5 (333)	98.5 (131)	99.2 (127)	97.4 (75)	.580
Cefixime, % (no.)	57.4 (194)	50.4 (67)	60.2 (77)	64.9 (50)	.088
Prednisolone, % (no.)	35.5 (120)	34.6 (46)	38.3 (49)	32.5 (25)	.674
Enoxaparin, % (no.)	39.9 (135)	38.4 (51)	42.2 (54)	39.0 (30)	.802

[a]BMI, body mass index; domiciliary low-flow O_2 therapy, oxygen administered when saturation was less than 93% at rest while breathing ambient air; COVID-19, coronavirus disease 2019; HCQ, hydroxychloroquine, 200 mg, 12 hours apart for the first 2 doses, then 200 mg/d for 5 or more days; oral cefixime, 400 mg/day for 5 or more days; oral azithromycin, 500 mg/day for 5 or more days; oral prednisolone or equivalents, range, 5 to 25 mg/day for 5 or more days; subcutaneous enoxaparin, 4000 IU/day for 5 or more days until mobilization or resolution of phlebitis.

[b]From February 28, according to Italian national policy, only patients presenting with more severe symptoms were tested using reverse transcriptase-polymerase chain reaction assay for severe acute respiratory syndrome coronavirus 2. Most patients treated at their domicile did not have access to the test.

[c]One-way analysis of variance: cut-off for *P* value interpretation after Bonferroni correction = .017.

Study End Points

During a median follow-up of 70 days (25%-75%; interquartile range, 55-76 days), 105 (31.1%) patients had a primary end point event (Figure 1A), that is, 18.8% (25/133) of normal-weight (BMI <25 kg/m^2), 17.2% (22/128) of overweight (25 kg/m^2 ≤BMI <30 kg/m^2), and 75.3% (58/77) of obese patients (BMI ≥30 kg/m^2; *P*<.0001 for both comparisons). Time to hospitalization was significantly shorter for obese compared with both normal- and overweight patients (Figure 1B).

In the crude unadjusted analysis, obese patients were more likely to require hospitalization than nonobese patients (BMI <30 kg/m^2; hazard ratio [HR], 6.21; 95% CI, 4.20 to 9.18). Male patients carried also higher risk (HR, 1.53; 95% CI, 1.01 to 2.31), while HCQ and prednisone use (HR, 0.68; 95% CI, 0.17 to 1.00; and HR, 0.59; 95% CI, 0.38 to 0.92, respectively) were less likely associated with the primary end point in the unadjusted analyses. In the final multivariable analysis, obese patients were more likely to need hospitalization than nonobese

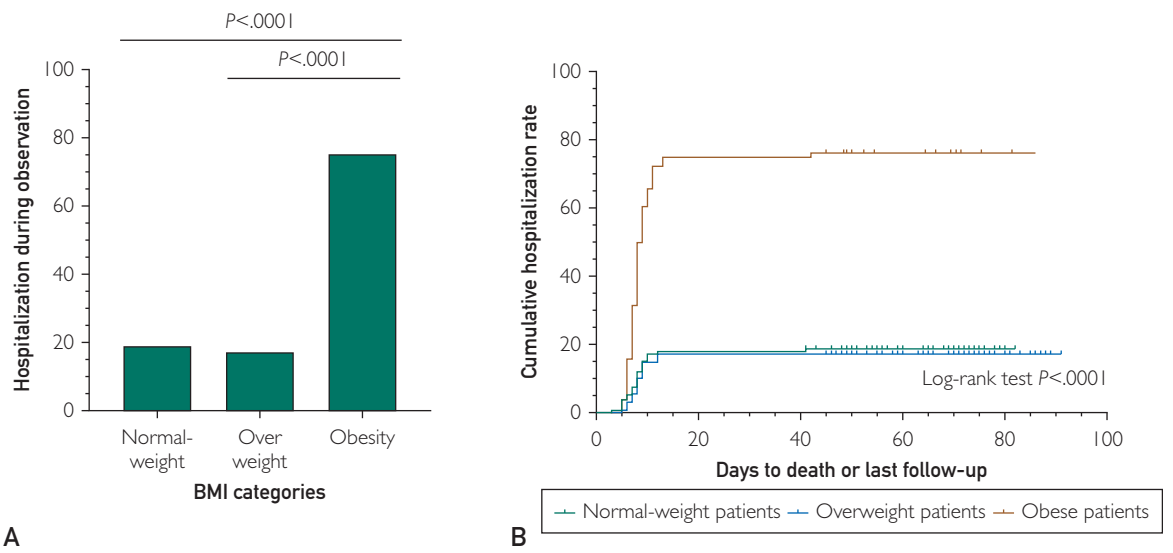

FIGURE 1. A, Association of body mass index (BMI) categories and hospitalization at the end of follow-up in the studied cohort of community-managed coronavirus disease 2019 (COVID-19) pneumonia. B, Time to hospitalization by BMI categories in the studied cohort of community-managed coronavirus disease 2019 pneumonia. Hospitalization rate in obese vs overweight and normal-weight patients was significantly increased at 10 days (65.8% vs 14.8% vs 17.3%; *P*<.0001), 30 days (75.0% vs 17.2% vs 17.3%; *P*<.001), and end of follow-up (75.3% vs 17.2% vs 18.8%; *P*<.0001).

patients (HR, 5.83; 95% CI, 3.91 to 8.71), without significant associations of other covariates (Figure 2). Results were similar in multiple sensitivity analyses (Supplementary Table, available online at http://www.mayoclinicproceedings.org).

Among secondary end points, domiciliary low-flow oxygen therapy was needed in 138 (40.8%) patients (Figure 3A), that is, 19.6% (26/133) of normal-weight, 39.8% (51/128) of overweight, and 79.2% (61/77) of obese patients. Hospitalization with NIV was needed in 76 (22.5%) patients (Figure 3B), that is, 11.3% (15/133) of normal-weight, 10.2% (13/128) of overweight, and 62.3% (48/77) of obese patients. Hospitalization in the intensive care unit with intubation was needed in 49 (14.5%) patients (Figure 3C), that is, 6.8% (9/133) of normal-weight, 5.5% (7/128) of overweight, and 42.9% (33/77) of obese patients. Death occurred in 9 (2.7%) patients and in all cases, patients died in the hospital, that is, 3.0% (4/133) of the normal-weight, 0% (0/128) of the overweight, and 6.5% (5/77) of the obese groups (Supplemental Figure 2A, available online at http://www.mayoclinicproceedings.org). Time to death significantly differed in the 3 categories (Log-rank test P=.0199) (Supplemental Figure 2B), significantly lower in obese compared with nonobese patients (P=.0184) (Figure 3D).

DISCUSSION

We reported the risk for hospitalization in patients with community-managed COVID-19 pneumonia by BMI categories, showing that obese patients were more likely to need hospitalization than nonobese patients. Moreover, obese patients had a more severe course, requiring domiciliary low-flow oxygen therapy, NIV, and intubation. Death due to COVID-19 was also higher in obese compared with nonobese patients.

Obesity is a recognized independent predictor of severe H1N1 infection,[19,20] and higher BMI has been inconsistently reported as a potential risk factor for severe outcomes of hospitalized patients with COVID-19

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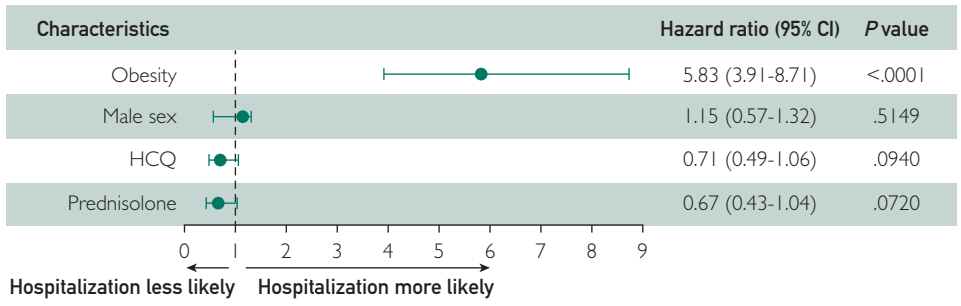

FIGURE 2. Adjusted hazard ratios of hospitalization in the final multivariable analysis. Shown are hazard ratios with 95% CIs from the final multivariable Cox proportional hazards model (model 1 of the Supplemental Table), which includes obesity with the additional covariates of sex (male), hydroxychloroquine (HCQ) use, and prednisolone use.

infection.[1,3,8-11] As for hospital cohorts,[12,13] the prevalence of obesity and overweight was high in community-managed patients with COVID-19 infection and was associated with worst prognoses. Interestingly, overweight/obesity and altered liver function were associated with the probability of prolonged hospitalization in patients with COVID-19 infection, highlighting the role of high BMI as a predictor of worst prognosis in hospitalized patients.[21]

In particular, in our cohort, obesity was associated with higher hospitalization risk and various degrees of respiratory impairment, as shown by the higher need of domiciliary low-flow oxygen therapy, NIV, and intubation during the observation period. This is consistent with several previous reports of hospitalized patients showing the association of obesity with invasive mechanical ventilation,[12,13] in-hospital mortality,[14] and an overall increased risk for critical illness during the disease course, as shown from a recent meta-analysis.[22]

Interestingly, higher BMI was associated with younger age at diagnosis. This was consistent with a previous observation from Johns Hopkins' hospitalized patients, showing that obesity can shift severe COVID-19 disease to younger individuals.[23] In community-managed patients, common comorbid conditions such as diabetes, hypertension, renal impairment, and cardiac and pulmonary diseases, which are recognized risk factors for severe COVID-19 infection, were not significantly associated with hospitalization. Consistently, obesity was the only variable associated with hospitalization in the final Cox regression analysis.

Although it is still possible that some amount of unmeasured confounding remains, the correction of the analysis for the most significant confounders and the consistency of results across sensitivity analyses is reassuring. Because the primary outcome of this study (i.e., hospitalization) is different from those of the previous hospital cohort studies (mostly intubation and/or in-hospital death), our findings suggest that pre-existing patient conditions driving hospitalization risk are likely different from those of poor outcomes in hospitalized patients.

This role of obesity in predisposing to worst outcomes in initially noncritical COVID-19 pneumonia leads to several practical considerations. First, for clinicians and patients, active vigilance and more aggressive management should be recommended for obese patients with COVID-19 pneumonia treated in a non-hospital setting. Second, because patients with higher BMI do not only have a higher hospitalization risk, but also a higher need of respiratory support, patients with BMI greater than 30 kg/m^2 might be preemptively hospitalized regardless of their clinical condition in the attempt to promptly intervene in case of respiratory or general complications.

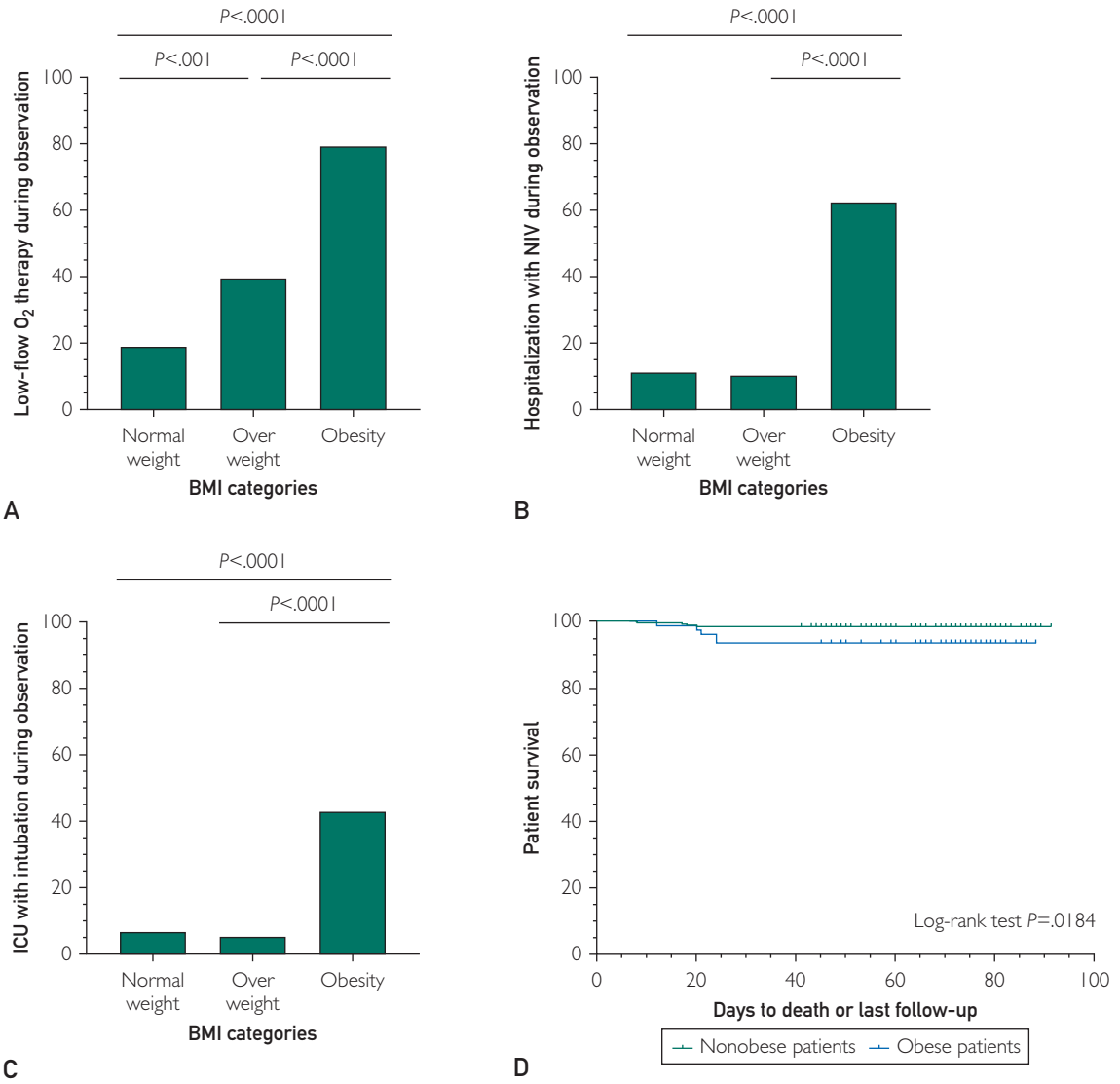

FIGURE 3. Association of body mass index (BMI) categories and (A) low-flow oxygen (O_2) need, (B) hospitalization with noninvasive ventilation (NIV), and (C) intubation at the end of follow-up in the studied cohort of community-managed coronavirus disease 2019 (COVID-19) pneumonia. (D) Time to death by BMI categories in the studied cohort of community-managed COVID-19 pneumonia. Overall, low-flow O_2 need, NIV, and intubation at the end of follow-up were significantly higher in obese compared with nonobese patients. Survival rates in obese vs nonobese patients were nonsignificantly different at 10 days (98.7% vs 99.6%; $P>.05$), while they were significantly different at 30 days (95.3% vs 98.5%; $P<.05$) and end of follow-up (93.6% vs 98.5%; $P<.05$). ICU, intensive care unit.

In non–COVID-19 clinical studies, obesity has been recognized as an independent predictor of acute respiratory distress syndrome in mechanically ventilated critically ill patients.[24] Several studies depicted obesity as a chronic low-grade inflammatory condition.[25,26] Others showed an effect on pulmonary function, affecting lung volumes and compliance and narrowing the peripheral airways.[27-30] Because angiotensin-converting enzyme type 2 is highly expressed in adipose tissue, more than in the lungs, it has been hypothesized that SARS-CoV-2 could be able to enter into

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adipocytes, which could become infected, thus contributing to the spreading to other organs, or represent a natural reservoir for the virus, thus leading to a prolonged viral clearence.[31] In addition, obesity may induce alteration in the renin-angiotensin system, promoting further derangement in COVID-19 infection.[31] Ultimately, several factors could contribute to explain the pathophysiology underlying this association, and further investigations are needed to clarify the link between obesity and severe COVID-19 infection.

Patients with mild or moderate COVID-19 infection are usually managed with supportive care at home.[32] Community-managed COVID-19 pneumonia, that is, patients with a moderate illness with clinical and radiologic signs of pneumonia, rely on acetaminophen, nonsteroidal anti-inflammatory drugs, azithromycin, HCQ, enoxaparin, and prednisone. No antiviral treatment or anti-cytokine monoclonal antibodies are used in this setting. No substantial difference has been observed in COVID-19 treatment across BMI categories, and in the multivariate analysis, no significant association between HCQ use and hospitalization has been observed. This result is in line with previous analyses of large cohorts of hospitalized patients, showing no protective effects of HCQ for intubation and/or in-hospital mortality, alone or in combination with azithromycin,[7,33] and with a recent randomized controlled trial showing that HCQ prophylaxis did not prevent illness after high to moderate risk exposure to SARS-CoV-2.[34]

Our data are subjected to several limitations. First, the observational retrospective design and extraction of data from nonstandardized medical records cannot completely exclude classification error and survivor treatment selection. However, given the direct involvement of general practitioners in collecting the data from their own patients and the relatively limited time of observation, we believe that these potential biases are minimal, if even present. The relatively limited availability of confirmatory testing due to the Italian Government restriction for RT-PCR in nonhospitalized patients could have led to ascertainment bias. However, all our patients were diagnosed using CT, which has sensitivity of 97% for the detection of COVID-19 pneumonia and has been proposed as a primary tool for COVID-19 detection in epidemic areas.[35] In addition, all tested patients were positive to RT-PCR for SARS-CoV-2, and ultimately, the inclusion of patients with indicative clinical pictures, yet not routinely tested for influenza and H1N1, is accepted in retrospective studies.[19] Finally, the results of this study may not reflect the risk factors for hospitalization in patients with COVID-19 infection without pneumonia and/or in patients of other communities with a different ethnic composition, such as those with high African American or Asian composition.[36]

CONCLUSION

Our findings showed that obese patients with community-managed COVID-19 pneumonia were more likely to require hospitalization and had an overall more severe course than nonobese patients. Obesity was the only factor among the pre-existing comorbid conditions and treatments for SARS-CoV-2 infection that associated with subsequent hospitalization in this community-managed cohort. Our findings should raise the level of awareness in clinicians and patients on the hospitalization risk in obese patients with COVID-19 pneumonia.

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SUPPLEMENTAL ONLINE MATERIAL

Supplemental material can be found online at http://www.mayoclinicproceedings.org. Supplemental material attached to journal articles has not been edited, and the authors take responsibility for the accuracy of all data.

Abbreviations and Acronyms: **BMI** = body mass index; **COVID-19** = coronavirus disease 2019; **CT** = computed tomography; **HCQ** = hydroxychloroquine; **HR** = hazard ratio; **ICU** = intensive care unit; **NIV** = noninvasive ventilation; **O_2** = oxygen; **RT-PCR** = reverse transcriptase–polymerase chain reaction; **SARS-CoV-2** = severe acute respiratory syndrome coronavirus 2

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