

Is Body Mass Index A Risk Factor in the Clinical Course of Patients with Coronavirus Disease 2019 Pneumonia?

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ABSTRACT

Objective: Coronavirus disease 2019 (COVID-19)-related infections emerging from China that spread worldwide show a wide range of clinical courses from asymptomatic presentation to respiratory failure and even death. Similar to non-COVID-19 infections, obesity, age, and comorbidities can also affect the clinical course of the disease. This study aimed to investigate the effect of obesity on the clinical course and mortality of patients hospitalized with COVID-19 pneumonia.

Methods: Between March 11 and April 30, 2020, patients hospitalized with COVID-19 pneumonia were retrospectively analyzed. Patients were classified as having severe and mild disease based on oxygen, non-invasive mechanical ventilation (NIMV), and invasive (IMV) mechanical ventilation requirements. Two groups were evaluated based on body mass index (BMI) of ≥ 25 and ≥ 30 kg/m².

Results: Of the 125 patients, 82 (65.6%) were men, and their mean age was 51.77 ± 4.99 years. Their mean BMI was 27.76 ± 4.76 kg/m². The difference of the mean BMI between the patients with severe and mild disease was statistically significant (28.8 ± 5.36 and 26.9 ± 4.10 , respectively) ($p=0.028$). BMI of ≥ 25 and ≥ 30 kg/m² were noted in 43.4% and 20.8% of patients with severe and mild disease, respectively, which was statistically significant ($p=0.007$). Moreover, 70.6% of 17 patients older than 65 years with BMI of ≥ 25 kg/m² had a severe clinical course ($p=0.021$). Among patients requiring NIMV, 59.1% and 31.8% had a BMI of ≥ 25 and 30 kg/m², respectively. Among patients requiring IMV, 66.7% and 37.5% had a BMI of ≥ 25 and 30 kg/m², respectively. No statistically significant difference was found between BMI and NIMV and IMV need. Death occurred in 14.8% of the patients. No statistically significant difference was found between the BMI of those who died and survived ($p=0.768$).

Conclusion: Our study showed that overweight and obesity were important factors in assessing and predicting disease severity, and special care should be taken in the follow-up of patients with a BMI of ≥ 30 kg/m².

INTRODUCTION

A new coronavirus, which first appeared in China and was highly contagious, has been spread worldwide since December 2019.^[1-5] The influenza-like virus that caused coronavirus disease 2019 (COVID-19) spread rapidly, with an average number of patient doubling every 7.5 days, and was declared as a pandemic by the World Health Organization (WHO) on January 13, 2020.^[3] The disease may differ from its asymptomatic form to pneumonia, acute respiratory distress, and mortality.^[6] The mortality of COVID-19 infection varies between 1.9% and 13.5% in publications reported from various countries.^[7,8]

Various factors affecting mortality have been reported in many published studies. Age, changes in markers of cytokine storm in blood parameters, radiological extent, and comorbidities are emphasized as factors affecting mortality.^[6] According to the first publications in the literature, besides advanced age, comorbidities, such as hypertension (HT), cardiovascular disease, diabetes, chronic respiratory disease, kidney disease, and cancer, have been reported as poor prognostic factors for COVID-19 infection.^[9]

Another comorbid condition that may affect the clinical course of many diseases, especially infectious diseases, is obesity.^[10] Epidemiological studies show that obesity in-

creases the risk of serious complications and death from influenza virus infections, especially in elderly individuals.^[11,12] Since the Spanish Flu epidemic in 1918, both malnutrition and obesity are associated with poor prognosis in viral infections.^[13] During the Influenza A H1N1 epidemic in 2009, obesity had been found to be associated with hospitalization, mortality, and risk of serious disease.^[14] Although it is related to poor prognosis, some studies have opposite results.^[15] In fact, studies have shown that obesity has no effect on prognosis in the clinical course of conditions, such as septic shock, cardiovascular surgery, acute coronary syndrome, and renal failure requiring dialysis.^[16–19] Some studies have reported that it reduces mortality.^[20–22] In addition, no significant relationship was found in terms of prognosis, with an increase in the risk of sepsis in morbid obesity.^[23]

Only few studies have investigated the role of obesity in the COVID-19 outbreak.^[24] This study aimed to investigate the effects of overweight and obesity on the clinical course and mortality of hospitalized patients with COVID-19 pneumonia.

MATERIALS AND METHODS

Patients with COVID-19 infection between March 11 and April 30, 2020 were examined retrospectively. Age, sex, and comorbidities were recorded from the patients' electronic and written files. Body mass index (BMI), which is calculated according to their height and weight during hospitalization, was also recorded. In addition, admission symptoms, non-invasive mechanical ventilation (NIMV) and invasive mechanical ventilation (IMV) needs, treatment regimens, discharge, and mortality were recorded.

According to the WHO classification, low BMI is defined as $<18.5 \text{ kg/m}^2$, overweight as $25\text{--}30 \text{ kg/m}^2$, and obese and morbid obesity as $\geq 30 \text{ kg/m}^2$.^[10] In our study, patients were divided into two groups: those with $\text{BMI} \geq 25 \text{ kg/m}^2$ (Group 1) and $\geq 30 \text{ kg/m}^2$ (Group 2). The course of the disease was evaluated according to these groups.

Patients with COVID-19 pneumonia were divided into two groups: those with severe and non-severe disease, according to the regularly updated guideline of the Scientific Board of the Ministry of Health of the Republic of Turkey.^[25]

Oxygen saturation in room air of $<90\%$, respiratory rate of $\geq 30/\text{min}$, widespread pneumonic infiltrations on chest X-rays and/or thoracic computed tomography, or detection of acute organ dysfunction was defined as severe disease. According to guideline suggestions, treatment with empirical combination of hydroxychloroquine and antiviral agents, with antibiotics when needed, was commenced for patients whose symptoms, radiology and history were compatible with COVID-19 pneumonia, pending swab PCR results. Yedikule Chest Diseases and Thoracic Surgery Training and Research Hospital Ethics Committee approved our study (date: 15.05.2020, no: 2020/5, 5/2).

Statistical analysis

Data were analyzed statistically using SPSS for Mac Version 20.00 (SPSS Inc., Chicago, IL., USA) package program. Continuous variables, such as age and BMI, were expressed as mean \pm standard deviation, and categorical variables, such as sex, disease course, and need for intensive care, were expressed as numbers and percentages (%). The consistency of continuous variables to normal distribution was evaluated using the Kolmogorov–Smirnov test. Based on the BMI, chi-squared test for categorical variables and Mann–Whitney U test and Student-t tests were used to compare obese and non-obese patients according to the categorical variables. Statistical significance was taken as $p < 0.05$.

RESULTS

Our study included 128 patients hospitalized with COVID-19 pneumonia. Three patients were excluded because their BMI was not recorded. The mean age of the patients was 51.77 ± 4.99 years. The patients comprised 82 (65.6%) and 43 (34.4%) men and women, respectively. At least one comorbidity was present in 82 (65.6%) patients, and the most common comorbidity was HT (30.4%). The mean BMI was $27.76 \pm 4.76 \text{ kg/m}^2$. The BMI of 88 (70.4%) and 38 (30.4%) patients was ≥ 25 and $\geq 30 \text{ kg/m}^2$, respectively. At least one comorbidity was present in 70.1% and 71% of patients with $\text{BMI} \geq 25$ and $\geq 30 \text{ kg/m}^2$. Table 1 shows the demographic characteristics of the patients.

No patient with a $\text{BMI} < 18.5 \text{ kg/m}^2$ was included in our study. However, two patients had a $\text{BMI} > 40 \text{ kg/m}^2$, and both patients needed intensive care and mechanical ventilation.

Table 1. Demographic features of patients

Number of patients	n=125
The average age, mean \pm SD	51.77 \pm 4.99
Gender, n (%)	
Female	43 (34.4)
Male	82 (65.6)
Comorbidity, n (%)	
No comorbidity	43 (34.4)
1 or more comorbidity	82 (65.6)
Hypertension	38 (30.4)
Chronic lung disease	23 (18.4)
Diabetes mellitus	20 (16)
Coronary artery disease	12 (9.6)
Malignancy	7 (5.6)
Hypothyroidism	6 (4.8)
BMI kg/m^2 , mean \pm SD	27.76 \pm 4.76
BMI $\text{kg/m}^2 \geq 25$, n (%)	88 (70.4)
BMI $\text{kg/m}^2 \geq 30$, n (%)	38 (30.4)

BMI: Body mass index; SD: Standard deviation.

Table 2. Evaluation of factors affecting the course of the disease

Variables	Severe disease (n=53)	Mild disease (n=72)	p-value
Gender, n (%)			
Male	38 (71.7)	44 (61.1)	0.218
Female	15 (28.3)	28 (38.9)	
Age (years), mean±SD	55.15±14.5	49.29±14.9	0.036
Age, n (%)			
<65	35 (66)	62 (86.1)	0.008
>65	18 (34)	10 (13.9)	
BMI (kg/m ²), mean±SD	28.8±5.36	26.9±4.10	0.028
BMI Group 1, n (%)			
Normal	13 (24.5)	24 (33.3)	0.287
Overweight and obese	40 (75.5)	48 (66.7)	
BMI Group 2, n (%)			
Normal	30 (56.6)	57 (79.2)	0.007
Obese	23 (43.4)	15 (20.8)	

BMI: Body mass index; SD: Standard deviation.

The severe group comprised 53 patients (42.4%). The mean BMI of the patients with severe and mild disease was 28.8 ± 5.36 and 26.9 ± 4.10 , respectively. The difference between the two groups was statistically significant ($p=0.028$). In 40 (75.5%) patients with severe disease, their BMI was ≥ 25 kg/m². In addition, 23 (43.4%) patients with BMI ≥ 30 kg/m² showed a severe clinical course, and BMI was statistically significant compared with those with <30 kg/m² ($p=0.007$) (Table 2).

The mean age of patients who died and those who survived was 64.8 ± 11.3 and 49.6 ± 14.5 years, respectively ($p<0.001$). In addition, 28 patients were >65 years. Of 17 patients >65 years with BMI ≥ 25 kg/m², 12 (70.6%) had a severe clinical course ($p=0.021$). Meanwhile, of 7 patients >65 years with BMI ≥ 30 kg/m², 5 (71.4%) had a severe clinical course ($p=0.646$).

NIMV was required in 22 patients (17.6%). Of these, the

BMI was ≥ 25 and ≥ 30 kg/m² in 13 (59.1%) and 7 (31.8%) patients, respectively. IMV was required in 24 (19.2%) patients. Of these, the BMI was ≥ 25 and ≥ 30 kg/m² in 16 (66.7%) and 9 (37.5%) patients, respectively. No statistically significant difference was found between BMI and NIMV and IMV needs (Fig. 1).

In our study, 18 (14.8%) patients died. The mean BMI of those who died and those who survived was 27.87 ± 4.68 and 27.51 ± 4.35 kg/m², which was found to have no statistical significant difference ($p=0.776$). Of those who died, 12 (66.6%) and 8 (44.4%) had a BMI of ≥ 25 and ≥ 30 kg/m², respectively. The mortality rate among patients with a BMI of ≥ 30 and ≥ 25 kg/m² was 21.1% and 13.6%, respectively (Fig. 1).

DISCUSSION

In this study, it was observed that patients with higher BMI may experience a more severe course. In addition, $>50\%$ of patients requiring NIMV cases had a BMI of ≥ 25 kg/m².

COVID-19 infection lead to many different clinical courses such as increased intensive care needs, high mortality rates and treatment costs according to the initial reports. The world is currently focusing on understanding the mechanism of the disease, researching new treatment options, and identifying data that can show a serious clinical course from the beginning and predict patients with a high mortality risk.

Although data on BMI was limited for patients with COVID-19 infection, they suggest that the role of obesity in the COVID-19 outbreak should not be overlooked. Various studies have shown that obesity can negatively affect the body's defense system against infections, and therefore overweight and obesity can be a risk factor for COVID-19-related mortality.^[26] Kassir^[27] concluded that higher BMI can be seen in patients with severe COVID-19 infection and non-survivors. Liu et al.^[28] reported that BMI was reported to be statistically higher (27.0 vs 22.0 kg/m²) in those with serious infections among 30 healthcare workers with COVID-19 pneumonia. In a retrospective analysis

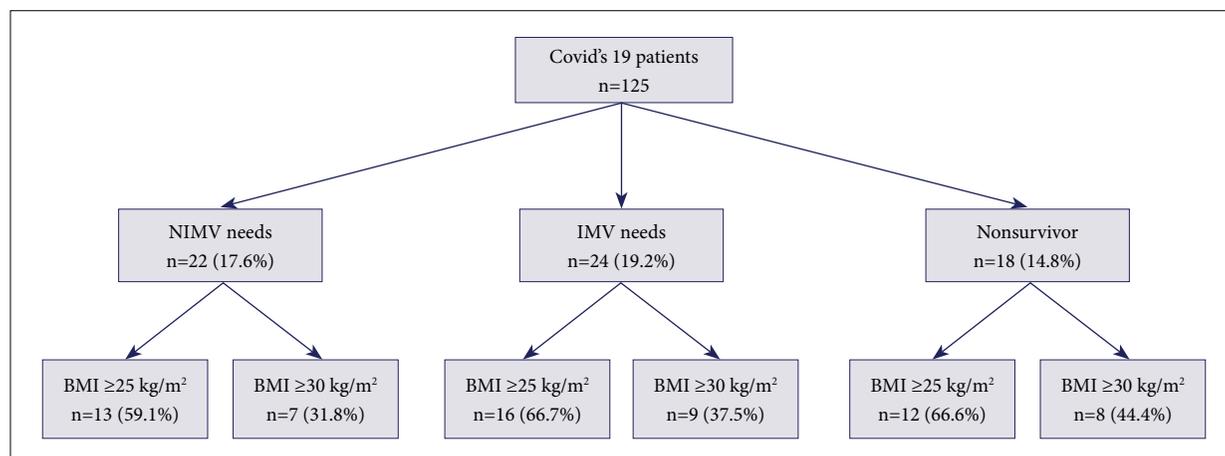


Figure 1. Distribution of Covid 19 patients according to clinical course.

on 112 patients with COVID-19 infection, the BMI (25.5 vs 22.0 kg/m²) of the critical group was significantly higher than that of the general group.^[24] In our study, patients with severe clinical course had higher BMI than those with mild clinical course (28.8 vs 26.9 kg/m²). In patients with BMI ≥ 30 kg/m², the disease showed a more severe clinical course with a statistical significance. When BMI is grouped as below and above 25 kg/m² in the same cohort, no statistically significant difference was found in patients with BMI ≥ 25 kg/m², although the disease shows a more severe clinical course.

Peng et al.^[24] showed that 15.18% of patients with COVID-19 infection died, and 88.2% of patients who died had BMI of ≥ 25 kg/m². In our study, the mortality rates were similar to those of Peng et al., and 66.7% of patients who died had a BMI of >25 kg/m².

Simonnet et al.^[29] observed that 85 (68.6%) of 124 patients who needed intensive care required IMV. The rate of obesity (BMI >30 kg/m²) and severe obesity (BMI ≥ 35 kg/m²) was 56.4% and 35.3% in patients requiring IMV. In our study, 37.5% of the patients requiring IMV had a BMI of ≥ 30 kg/m².

Hypertension and diabetes, which are more common in old age, are associated with stiffness in the vessels and impaired metabolic response. Older people (for example age >70 years) have diminished cardiopulmonary reserve to deal with COVID-19 infection compared with younger individuals.^[9] In our study, 70.6% of the patients who were >65 years with BMI ≥ 25 kg/m² had a severe clinical course. This rate was statistically significantly higher compared with those >65 years and those with BMI <25 kg/m² ($p=0.021$). Our results supported that COVID-19 infection was more severe in patients with older age and concurrent obesity.

The immune system, which plays an important role in the pathogenesis of COVID-19 infection, is also crucial in increased inflammation due to obesity. This inflammation of the adipose tissue potentially results in dyslipidemia, insulin resistance, type 2 diabetes mellitus (DM), HT, and metabolic dysfunction, leading to cardiovascular disease.^[29] The U.S. Center for Disease Control reported that of the 1482 patients who were hospitalized because of COVID-19 infection, 89.3% had ≥ 1 comorbidities, and the most common comorbidities were HT (49.7%), obesity (48.3%), chronic lung disease (34.6%), DM (28.3%), and cardiovascular diseases (27.8%). A positive correlation was found between overweight and obesity and the frequency of comorbidities.^[30] In our study, 65.6% of patients had more than one comorbidity. The most common comorbidities were HT, DM, and chronic lung diseases. In our study, at least one comorbidity was present in 70.1% and 71% of patients with BMI ≥ 25 and ≥ 30 kg/m², respectively, and at a higher rate compared with all our patients.

The limitations of our study include; its single-centered and retrospective design. Only a limited number of patients were included, and records related to body fat ratio and waist circumference in addition to BMI were not found. In addition, because the BMI of our overweight pa-

tients ranged mostly between 25 and 35 kg/m², sufficient data on morbidly obese patients could not be provided. Our study showed that various risk factors may have an effect on mortality in COVID-19 pneumonia. Although performing regression analysis would be beneficial to determine independent risk factors, this analysis could not be performed due to the small sample size.

CONCLUSION

In conclusion, this cohort study showed that overweight and obesity are important factors in evaluating and predicting disease severity, and caution be taken, especially in the follow-up of patients with BMI ≥ 30 kg/m². In the presence of overweight, advanced age, and comorbidity, the disease may be more severe, and the need for IMV may be higher in this group, and close follow-up of these patients should be considered. Larger case series are needed to obtain more precise results.

Ethics Committee Approval

Approved by the Yedikule Chest Diseases and Thoracic Surgery Training and Research Hospital Ethics Committee (date: 15.05.2020 no: 2020/5, 5/2).

Peer-review

Internally peer-reviewed.

Authorship Contributions

Concept: D.T., M.Ç., E.Ç.; Design: M.A.Ö., E.G.U.C., B.Z.Y., D.T.; Supervision: E.Ç., H.Ç., E.T.; Materials: E.T., M.Ç., E.G.U.C., B.Z.Y.; Data: D.T., E.T., E.G.U.C., B.Z.Y.; Analysis: M.A.Ö., H.Ç.; Literature search: M.Ç., D.T., E.Ç.; Writing: D.T., E.T.; Critical revision: H.Ç., E.Ç.

Conflict of Interest

None declared.

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COVID-19 Pnömonisi Olan Hastaların Klinik Seyrinde Vücut Kitle İndeksi Bir Risk Faktörü Mü?

Amaç: COVID-19 pandemisi Çin'den başlayarak hızla tüm dünyaya yayılmış ve asemptomatik formdan solunum yetersizliği ve mortaliteye kadar giden geniş bir yelpazede klinik seyir göstererek pek çok ülkede sağlık sisteminde önemli derecede zorlanmalara neden olmuştur. COVID-19 dışı enfeksiyonlara benzer olarak, yaş ve komorbiditeler gibi obezite de hastalığın klinik seyrini etkileyebilir. Çalışmamızda COVID-19 pnömonisi ile takip edilen hastalarımızda kilolu olmanın ve obezitenin, hastalığın klinik seyri ve mortalite üzerine etkisinin araştırılması amaçlanmıştır.

Gereç ve Yöntem: 11 Mart–30 Nisan 2020 tarihleri arasında COVID-19 enfeksiyonlu hastalar geriye dönük olarak incelendi. Hastaların elektronik ve yazılı dosyalarından yaş, cinsiyet, ek hastalıkları, vücut kitle indeksleri (VKİ), noninvaziv mekanik ventilasyon (NIMV) ve invaziv mekanik ventilasyon (İMV) ihtiyaçları ve mortalite durumları kaydedildi. O₂ ihtiyaçları, NIMV, İMV ihtiyaçlarına göre ağır ve hafif klinik seyirli iki gruba ayrıldı. Hastalar BMI ≥ 25 kg/m² ve ≥ 30 kg/m² olarak iki gruba ayrılarak hastalığın seyri değerlendirilmiştir.

Bulgular: Çalışmaya dahil edilen 125 olgunun 82'si (%65.6) erkek ve yaş ortalaması 51.77 \pm 4.99 idi. VKİ ortalaması 27.76 \pm 4.76 kg/m² idi. Ağır ve hafif seyirli hastaların VKİ ortalaması arasındaki fark istatistiksel olarak anlamlıydı (sırasıyla, 28.8 \pm 5.36 ve 26.9 \pm 4.10) (p=0.028). Ağır seyirli olguların %43.4'ünün VKİ ≥ 30 kg/m² iken hafif klinik seyirli olguların %20.8'i VKİ ≥ 30 kg/m² idi ve istatistiksel olarak anlamlıydı (p=0.007). Altmış beş yaşının üzerinde ve VKİ ≥ 25 kg/m² olan 17 hastanın %70.6'sı ağır klinik seyir göstermişti (p=0.021). NIMV ihtiyacı olan hastaların %59.1'inin VKİ ≥ 25 kg/m², %31.8'inin VKİ ≥ 30 kg/m² dir. İMV ihtiyacı olan hastaların %66.7'inin VKİ ≥ 25 kg/m², %37.5'inin VKİ ≥ 30 kg/m² dir. VKİ ile NIMV ve İMV ihtiyacı arasında istatistiksel olarak anlamlı fark bulunamadı. Hastaların %14.8'i hayatını kaybetti. Hayatını kaybeden ve yaşayan olguların VKİ'leri arasında istatistiksel olarak anlamlı fark yoktu (p=0.768).

Sonuç: Bu kohort çalışması, aşırı kilo ve obezitenin hastalık şiddetini değerlendirmede ve tahminde önemli bir faktör olduğunu ve özellikle VKİ ≥ 30 kg/m² olan hastaların takiplerinde dikkatli olunması gerektiğini göstermiştir.

Anahtar Sözcükler: Ciddi hastalık; COVID-19; vücut kitle indeksi.