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Clinical Characteristics and Outcomes of COVID-19 Patients with Overweight and Obesity: Turkish Nationwide Cohort Study (TurCObesity)

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ABSTRACT

Purpose While obesity is related to more severe outcomes of coronavirus disease 2019 (COVID-19), factors leading to poor prognosis still remain unclear. The present study evaluated the outcomes of COVID-19 patients who were overweight or obese and variables associated with severe disease in a large group of consecutive cases.

Methods A nationwide retrospective cohort study was performed using the Turkish National Healthcare Database. Demographic characteristics, laboratory tests, comorbidities, and medications of patients registered between March 11 and May 30, 2020, were recorded.

Results A total of 14,625 patients (median age:42, IQR:26 years; female 57.4 %) with normal weight (34.7 %), overweight (35.6 %), and obesity (29.7 %) were included. Hospitalization,

ICU admission, intubation/mechanical ventilation, pulmonary involvement, and mortality were significantly higher in patients who were overweight or obese. In adjusted analyses, both overweight (OR, 95 % CI: 1.82, 1.04–3.21; p = 0.037) and obesity (OR, 95 % CI: 2.69, 1.02–1.05; p < 0.001) were associated with a higher intubation/mechanical ventilation rate but only obesity was associated with increased mortality (OR, 95 % CI: 2.56, 1.40–4.67; p = 0.002). Old age, male gender, chronic kidney disease, and high C reactive protein levels were independently associated with COVID-19 mortality in overweight or obese patients.

Conclusions COVID-19 patients who were overweight or obese were more likely to have adverse outcomes but only obesity was a predictor of mortality. Such patients should receive urgent medical attention and active management, especially the elderly, men, and people with chronic kidney disease.

Introduction

The new coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus (SARS-CoV-2) which was initially identified in Wuhan, China. COVID-19 then spread to all countries in the world and was declared a pandemic by the World Health Organization (WHO) on March 11, 2020. On the same day, the Turkish Ministry of Health announced the first case of COVID-19 infection in Turkey and the disease spread rapidly throughout the country, as in many other countries. The disease has caused many adverse outcomes as of March 25, 2021, and has resulted in more than 30 000 confirmed deaths in Turkey [1].

Early studies from China, South Korea, and Singapore showed that clinical outcomes of hospitalized COVID-19 patients were pneumonia, shock, acute respiratory distress syndrome (ARDS), acute cardiac injury, acute kidney injury, and death [2–4]. The highest relative risk of death due to COVID-19 was observed in the elderly, male sex, and individuals with hypertension, diabetes mellitus, obesity, and underlying medical conditions [5]. The critical role of obesity in a detrimental disease course was first observed in China with an increased risk of developing severe pneumonia in patients who were overweight (86 %) or obese (140 %) during COVID-19 infection [6].

Subsequently, the accumulating data from all over the world indicated obesity as one of the major independent risk factors for adverse outcomes of COVID-19 infection [7], including hospitalization, ICU admission, invasive mechanical ventilation, and mortality [8, 9]. However, the relatively small sample size in some studies, uncontrolled or complicated co-morbidities like diabetes mellitus, cardiovascular disease (CVD), hypertension, and kidney disease most often confound the results or at least complicate our understanding of the independent role of obesity in moderate to adverse clinical outcomes [10, 11]. Even the analysis of large databases showed heterogeneous results regarding the association between body mass index (BMI) and COVID-19 mortality. For example, according to the Kaiser Permanent Database from the United States of America (USA), relative to normal weight, there is a significant association between BMI > 40 kg/m^2 and increased risk of mortality [12] whereas the OpenSAFELY registry from England showed BMI > 30 kg/m^2 as the threshold for a similar association [8]. However, the factors involved in the increased risk of adverse outcomes of COVID-19 in obese individuals have not been studied sufficiently.

In this context, additional information and further analysis are needed for a better understanding of the relationship between obesity and clinical outcomes of COVID-19 infection and to identify the most vulnerable phenotypes of patients who are overweight or obese. In this study, we used a large database with an aim to elucidate the relationship between patient characteristics and adverse outcomes in COVID-19 patients with overweight and obesity.

Material and Methods

Study design and participants

This population-based study was conducted using the data collected in the Turkish National Healthcare Database (TNHD) that covers the public health insurance of more than 95 % of the population in Turkey. To promote data sharing with the scientific society, demographic, clinical, and outcome data of all symptomatic confirmed cases of COVID-19 infection were made available to the author group under the supervision of the Ministry of Health, and several publications have been made so far [13, 14]. The present study was approved by the COVID-19 Investigation Review Board (IRB) under the General Directorate of Health Services Bioethics Committee designated by the Ministry of Health, which waived the requirement of informed consent due to the retrospective study design and anonymity of the TNHD database (IRB no: 95741342–020/27112019).

The study population included patients aged 18 years or older (n = 149 671) with a diagnosis of COVID-19 between 11 March and 30 May 2020. Only patients with a confirmed diagnosis through positive SARS-CoV-2 polymerase-chain-reaction (PCR) test and having a recent BMI information (on admission or within 3 months prior to the admission) available in the system were included. A consort diagram illustrating patient enrollment is given in ▶ **Fig. 1**. Briefly, patients who were younger than 18 years, still hospitalized at the time of data analysis, and without relevant BMI data were excluded (n = 135 046). Patients with BMI < 18.5 kg/m^2 were not studied as there were almost no associated records in the database. The remaining patients (n = 14 625) were stratified into three groups as normal weight, overweight, and obesity.

Data collection

Sociodemographic information (age, gender, BMI, smoking, and education), on admission laboratory test results (blood glucose, estimated glomerular filtration rate [e-GFR]), lipids (low- and high-density lipoprotein cholesterol [LDL-C and HDL-C], total-C, and triglycerides), alanine and aspartate aminotransferases (ALT and AST), C-reactive protein (CRP), D-dimer, procalcitonin, lactate dehydrogenase (LDH), ferritin, fibrinogen, lymphocyte count), chest CT findings on admission consistent with COVID-19, comorbid diseases including diabetes mellitus, hypertension, dyslipidemia, asthma/chronic obstructive

pulmonary disease (COPD), heart failure, CVD, chronic kidney disease, and cancer, and information on the use of medications like renin-angiotensin system (RAS) blockers, statin, and acetylsalicylic acid were obtained from TNHD.

Definitions

BMI was calculated as the ratio of weight to the square of height (kg/m^2). Normal weight was defined as having BMI values between 18.5 and 24.9 kg/m^2, overweight and obese individuals had BMI between 25 and 29.9 kg/m^2, and 30 kg/m^2 or over, respectively. We further defined a subgroup of BMI ≥ 40 kg/m^2 as morbid obesity. Smoking was defined as current smoking. Higher education was defined as having attained formal education for nine years and more. Diabetes, hypertension, dyslipidemia, COPD, asthma, heart failure, coronary artery disease, peripheral artery disease, and cerebrovascular disease were defined based on the ICD-10 codes. The latter three diseases are defined as CVD. Chronic kidney disease was defined as a reduced e-GFR < 60 mL/min/1.73 m^2 according to the Chronic Kidney Disease Epidemiology Collaboration equation.

Study outcomes

The primary outcome was mortality. The secondary outcomes were hospitalization and intubation/mechanical ventilation during hospitalization.

Statistical analyses

Data were analyzed using the SPSS Statistics for Windows 25.0 (SPSS Inc. 111 Chicago, IL). Continuous data were presented as mean (standard deviation: SD) or median (interquartile range: IQR) as appropriate. Categorical variables were summarized as counts (n) of all patients and percentages (%). The normality of data distribution was tested using the Kolmogorov-Smirnov test. Between-group differences were assessed using the Chi-square test, the Student's t-test, or the Mann-Whitney U test, as appropriate. Simple and multiple logistic regression analyses were performed to explore whether being overweight or obese was associated with hospitalization, length of hospital stay, ICU admission, mechanical ventilation, and mortality variables with the significant univariate association, and the outcomes were entered into the multiple logistic regression model. Stratified analyses were also performed according to age (≥ 65 or < 65 years) and gender. Statistical significance was set at a p-value ≤ 0.05.

Results

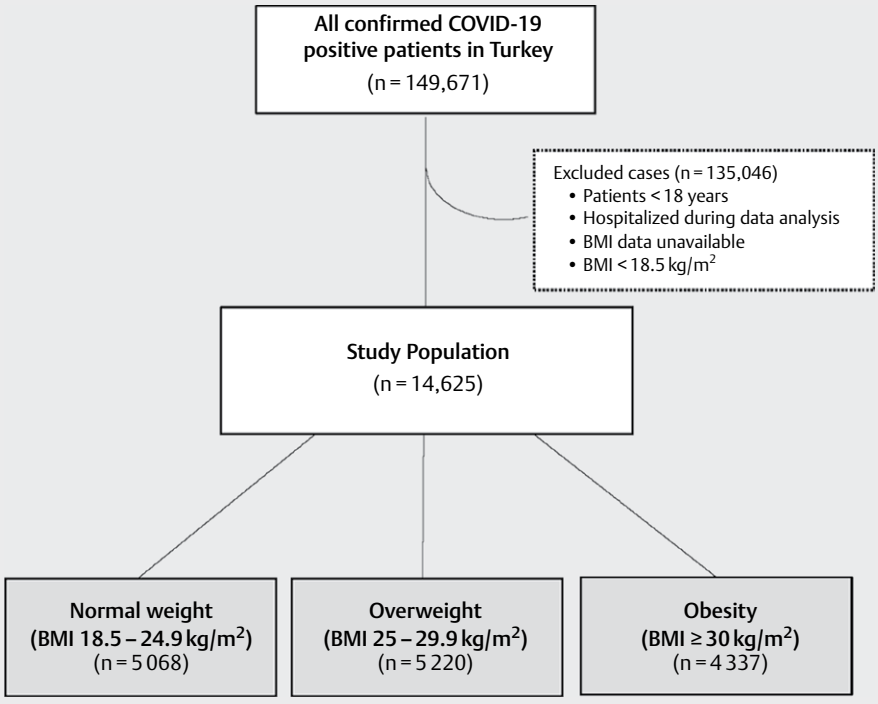
A total of 14,625 patients (age median: 42, IQR: 26; female: 57.4 %) were included. The study population consisted of 5068 (34.7 %) patients with normal weight, 5220 (35.6 %) overweight patients, and 4337 (29.7 %) patients with obesity. In addition, 2.7 % (n = 397) of patients were severely obese (BMI > 40 kg/m^2). Demographic, clinical, and laboratory characteristics of the patients are mentioned in ▶ **Table 1**. There were significant differences in median age, gender, smoking rates, and education levels across all BMI classes (p < 0.001 for all). The proportion of female patients was higher in the obesity group compared to those in the overweight and normal-weight groups (p < 0.05), but there were fewer women in the overweight group than in the normal-weight group (p < 0.05). Patients in the obesity group were significantly older than those in the overweight and normal-weight groups (p < 0.05 for both). Overweight patients were also older than the normal weight patients (p < 0.05). However, the median ages at death were significantly higher for patients in the normal weight group compared to those in the overweight (p = 0.01), obesity (p = 0.013), and morbid obesity (p = 0.003) groups (▶ **Fig. 2**).

The rate of overall mortality as the primary endpoint was 3.2 %, which increased from 1.4 % in the normal-weight group to 3.6 % and 4.7 % in overweight and obesity groups, respectively (p < 0.001) (▶ **Table 1**). Between-group differences in obesity vs. overweight and overweight vs. normal weight classes were also significant (p < 0.05). The rate of hospitalization, the longer length of hospital stays (> 8 days median), ICU admission, intubation, and pulmonary involvement on CT were significantly higher in overweight and obesity groups relative to the normal weight group (p < 0.001 for all). The rate of hospitalization and the longer length of hospital stay in the obesity group were also higher than those in the overweight group. Numeric increase in the rates of ICU admission, intubation, and pulmonary involvement on chest CT in the obesity group, compared to those of the overweight group was not statistically significant (▶ **Table 1**). The rate of hospitalization, the longer length of hospital stay, ICU admission, intubation, and death rates were significantly higher in the overweight group compared to those in the normal weight group (p < 0.05) (▶ **Table 1**).

As expected, the proportion of comorbid conditions and medication use gradually increased from the normal weight group to the overweight and obesity groups (▶ **Table 1**). The levels of glucose, e-GFR, HDL-C, total-C, triglycerides, AST, ALT, CRP, D-dimer, LDH, ferritin, fibrinogen, and the proportion of low lymphocyte count significantly different across the three BMI classes (p < 0.05 for all). Also, comorbid conditions and the use of RAS blockers, statins, and acetylsalicylic acid differed significantly (p < 0.001 for all) (▶ **Table 1**).

Multivariable logistic regression analysis revealed that obesity (OR: 2.56, 95 % CI: 1.40–4.67, p = 0.002) and morbid obesity (OR: 3.88, 95 % CI: 1.40–10.80, p = 0.009) were independently associated with mortality, along with older age (OR: 1.07, 95 % CI: 1.06–1.04, p < 0.001), male gender (OR: 2.45, 95 % CI: 1.63–3.70, p < 0.001), elevated CRP levels (OR: 3.35, 95 % CI: 1.82–6.17, p < 0.001), pulmonary involvement on CT (OR: 1.48, 95 % CI: 1.01–2.17, p = 0.046), and chronic kidney disease (OR: 2.38, 95 % CI: 1.56–3.65, p < 0.01) (▶ **Table 2**). In the fully adjusted model, many variables including overweight (OR: 1.82, 95 % CI: 1.04–3.21, p = 0.037), obesity (OR: 2.69, 95 % CI: 1.51–4.76, p = 0.001), morbid obesity (OR: 2.86, 95 % CI: 1.08–7.59, p = 0.035), older age (OR: 1.04, 95 % CI: 1.02–1.05, p < 0.001), male gender (OR: 1.60, 95 % CI: 1.11–2.30, p = 0.011), elevated CRP levels (OR: 2.25, 95 % CI: 1.40–3.62, p = 0.001), pulmonary involvement on CT (OR: 1.80, 95 % CI: 1.26–2.57, p = 0.001), and chronic kidney disease (OR: 1.96, 95 % CI: 1.29–2.96, p = 0.001) showed significant association with intubation.

Analyses after stratification according to BMI categories showed an independent association of old age with mortality (OR: 1.11, 95 % CI: 1.06–1.17, p < 0.001) in patients with normal weight. In the overweight patients, older age (OR: 1.07, 95 % CI: 1.04–1.11, p < 0.001), male gender (OR: 2.49, 95 % CI: 1.21–5.14, p = 0.013),



▶ **Fig. 1** A consort diagram presenting patient enrollment in the study.

heart failure (OR: 2.49, 95 % CI: 1.08–5.70, p = 0.031), chronic kidney disease (OR: 2.17, 95 % CI: 1.05–4.48, p = 0.037), cancer (OR: 2.85, 95 % CI: 1.25–6.52, p = 0.013), and elevated CRP levels (OR: 3.05, 95 % CI: 1.11–8.35, p = 0.03) were independently associated with mortality. In patients with obesity, older age (OR: 1.06, 95 % CI: 1.03–1.09, p < 0.001), male gender (OR: 2.53, 95 % CI:1.45–4.41, p = 0.001), chronic kidney disease (OR: 3.88, 95 % CI:2.11–7.16, p < 0.00), and elevated CRP levels (OR: 3.36, 95 % CI:1.45–7.79, p = 0.005) were independently associated with mortality (▶ **Table 3**).

Age-stratified analysis showed that obesity was independently associated with mortality in patients younger (OR: 3.53, 95 % CI: 1.63–7.66, p < 0.001) or older (OR: 1.72, 95 % CI: 1.06–2.81, p = 0.030) than 65 years of age (▶ **Fig. 3**). Sex stratified analyses showed that obesity was independently associated with mortality in both women and men (OR: 2.16, 95 % CI: 1.28–3.64, p = 0.004) (▶ **Table 4**).

Discussion

In this study on a large patient population with a confirmed diagnosis of COVID-19 (positive SARS-CoV-2 by PCR test), two-thirds of the patients were overweight or obese. We found that obesity and morbid obesity were significantly related to higher mortality among COVID-19 patients. However, this relationship was not observed among overweight patients. Obese and overweight patients were at equally increased risk of intubation. The association of obesity with death was consistent across all age groups but it was more robust in younger patients. The odds of the association between obesity and mortality were similar among women and men. We used the data collected from all seven geographical regions of Turkey and no additional patient inclusion criterion was applied other than the availability of BMI information, therefore, the current results can be accepted as representative of the entire country.

Several different mechanisms have been proposed to explain the potential role of obesity in the more adverse course of COVID-19. Obesity has been found to be related to reduced immune response and worsened prognosis in patients with a pulmonary disease [15]. Obesity also has negative effects on respiratory function, because it may lead to mechanical compression of the lung, bronchus, and diaphragm [16]. More specifically, augmented expression of angiotensin-converting enzyme 2 in obesity may increase the binding of the viral S protein to the adipose tissue and make it a portal for virus invasion [17]. Obesity may also lead to ectopic accumulation of adipocytes within the alveolar interstitial space that may cause direct viral infection and aggravate the inflammatory response, and contribute to the massive interstitial edema [18]. However, factors related to demographic characteristics, laboratory abnormalities, comorbidities, or medications that may contribute to poor outcomes in obese patients with COVID-19 need to be studied.

Studies worldwide have reported different morbidity and mortality rates for COVID-19. France and the United Kingdom reported a higher mortality rate of ~10 %, while that in other countries like India, Israel, and Russia has been reported to be less than 2 % [19–24]. A study from the USA reported the mortality rate to be as high as 39.6 % among the hospitalized older (> 50 years old) morbidly obese patients with COVID-19 [25]. A recent study from Korea

▶ **Table 1** Basic characteristics of patients diagnosed with new coronavirus disease 2019 (COVID-19) categorized according to weight.

	Total patients (n = 14625)	**Available data (n)**	**Patients with normal weight (n = 5068, 34.7%)**	**Overweight patients (5220, 35.7%)**	**Patients with obesity (n = 4337, 29.7%)**	**p**
Age, years, median (IQR)	42 (26)	14625	32 (18)[a,b]	45 (24)[c]	51 (22)	**<0.001**
Gender, female, n (%)	8393 (57.4)	14625	2789 (55.0)[a,b]	2578 (49.4)[c]	3026 (69.8)	**<0.001**
Smoking, current, n, (%)	2272 (21.7)	10479	989 (26.3)	803 (21.3)	480 (16.2)	**<0.001**
Education, >8 years, n, (%)	4579 (40.1)	11409	2181 (52.8)	1625 (39.7)	773 (24.3)	**<0.001**
BMI, kg/m^2, median (IQR)	27.05 (7.09)	14625	22.50 (3.30)	27.34 (2.41)	33.2 (4.75)	**<0.001**
Comorbidities						
Diabetes mellitus, n (%)	4261 (29.5)	14422	660(13.1)	1489 (28.9)	2112 (49.7)	**<0.001**
Hypertension, n (%)	6039 (41.3)	14625	1160 (22.9)	2201 (42.2)	2678 (61.7)	**<0.001**
Dyslipidemia, n (%)	3070 (21.0)	14625	490 (9.7)	1162 (22.3)	1418 (32.7)	**<0.001**
Asthma/COPD, n (%)	3344 (22.9)	14625	813 (16.0)	1194 (22.9)	1337 (30.8)	**<0.001**
Heart failure, n (%)	588 (4.0)	14625	89 (1.8)	213 (4.1)	286 (6.6)	**<0.001**
CVD, n (%)	2809 (19.2)	14625	521 (10.3)	1049 (20.1)	1239 (28.6)	**<0.001**
Chronic kidney disease, n (%)	551 (13.7)	4025	109 (9.5)	204 (13.8)	238 (17.0)	**<0.001**
Cancer n (%)	619 (4.2)	14625	166 (3.3)	221 (4.2)	232 (5.3)	**<0.001**
Clinical severity						
Hospitalization, n (%)	7100 (48.5)	14625	2018 (39.8)[a,b]	2634 (50.5)[c]	2448 (56.4)	**<0.001**
Hospital stay, >8 days, n (%)	3285 (46.3)	7100	822 (40.7)[a,b]	1267 (48.1)[c]	1196 (48.9)	**<0.001**
ICU admission, n (%)	873 (12.3)	7092	168 (8.3)[a,b]	355 (13.5)	350 (14.3)	**<0.001**
ICU stay >5 days, n (%)	414 (47.5)	871	73 (43.5)	169 (47.7)	172 (49.3)	0.459
Intubation, n (%)	531 (7.5)	7092	98 (4.9)[a,b]	213 (8.1)	220 (9.0)	**<0.001**
Chest CT on admission consistent with COVID-19, n (%)	3535 (26.1)	13541	794 (17.3)	1380 (28.4)	1361 (33.3)	**<0.001**
Death, n (%)	465 (3.2)	14625	72 (1.4)[a,b]	190 (3.6)[c]	203 (4.7)	**<0.001**
Laboratory values						
Glucose, mg/dL, median (IQR)	103 (38)	3705	96 (23)	104 (37)	111 (49)	**<0.001**
e-GFR, mL/min/1.73 m^2, median (IQR)	103 (48)	4243	114.3 (47.6)	100.8 (44.4)	97.6 (43.3)	**<0.001**
LDL-C, mg/dL, median (IQR)	116.8 (51.4)	669	112 (53)	115 (58)	119 (44)	0.599
HDL-C, mg/dL, median (IQR)	46 (20)	719	53 (24)	45 (19)	46 (18)	**<0.001**
Total-C, mg/dL, median (IQR)	191 (62)	663	185 (66)	191 (66)	199 (53)	**0.044**
Triglycerides, mg/dL, median (IQR)	132.1 (91.6)	818	107 (78)	138 (96)	140 (89)	**<0.001**
AST, >ULN, n (%)	309 (17.1)	1803	47 (9.5)	130 (19.3)	132 (20.8)	**<0.001**
ALT, >ULN, n (%)	329 (18.0)	1828	60 (12.1)	135 (19.6)	134 (20.8)	**<0.001**
CRP, >ULN, n (%)	1923 (60.6)	3172	467 (49.4)	699 (61.2)	757 (69.9)	**<0.001**
D-dimer >ULN, n (%)	422 (44.9)	940	96 (35.7)	159 (43.9)	167 (54.0)	**<0.001**
Procalcitonin, >ULN, n (%)	51 (13.6)	375	12 (12.2)	22 (14.6)	17 (13.5)	0.871
Lactate dehydrogenase, >ULN, n (%)	619 (38.3)	1617	127 (28.7)	236 (38.5)	256 (45.6)	**<0.001**
Ferritin, >100 ng/mL, n (%)	810 (51.9)	1562	180 (39.0)	333 (57.6)	297 (56.8)	**<0.001**
Fibrinogen, >ULN, n (%)	158 (71.8)	220	26 (57.8)	76 (71.0)	56 (82.4)	**0.017**
Lymphopenia, Lym#<1000, n (%)	1243 (16.9)	7339	354 (15.3)	502 (18.7)	387 (16.5)	**0.005**

▶ **Table 1** Continued.

	Total patients (n = 14625)	Available data (n)	Patients with normal weight (n = 5068, 34.7 %)	Overweight patients (5220, 35.7 %)	Patients with obesity (n = 4337, 29.7 %)	p
Medications						
RAS blocker, n (%)	3617 (24.7)	14625	511 (10.1)	1313 (25.2)	1793 (41.3)	**< 0.001**
Statin, n (%)	1588 (10.9)	14625	211 (4.2)	604 (11.6)	773 (17.8)	**< 0.001**
Acetylsalicylic acid, n (%)	2237 (15.3)	14625	383 (7.6)	827 (15.8)	1027 (23.7)	**< 0.001**

(COPD, chronic obstructive pulmonary disease; CVD, cardiovascular disease; CT, computerized tomography; e-GFR, estimated glomerular filtration rate; LDL-C and HDL-C, low- and high-density lipoprotein cholesterol; total-C, total cholesterol; and triglycerides); ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRP, C-reactive protein; LDH, lactate dehydrogenase; RAS, renin-angiotensin system; ULN, upper limit of normal).

demonstrated a non-linear (U-shaped) relationship between BMI and fatal illness, wherein, subjects with a BMI ≥ 25 kg/m^2 had a high risk of fatal outcomes [26]. In our study, the overall mortality rate was 3.2 %, although we observed a significantly increased mortality in both overweight (3.6 %) and obese (4.7 %) groups compared to that in the normal weight group (1.4 %). These results suggest that death due to COVID-19 in patients with or without obesity was relatively low in the present study. Possible explanations for the low mortality rate may be that the national health care system of Turkey covers all citizens and standard treatment protocols developed by the National Scientific Advisory Committee were implemented for all patients with COVID-19 during the earliest phase of the pandemic. Moreover, our healthcare system did not face significant overload during the COVID-19 outbreak. Importantly, while most other studies were carried out on hospitalized patients, our study included both outpatients and inpatients. The relatively younger age of our study population (median age: 42, IQR: 26 years) may be associated with the low mortality rate as well.

Determinants of mortality in COVID-19 infection have already been evaluated in studies from different countries. Obesity in COVID-19 patients has been found to be an independent predictor of worse clinical outcomes and may lead to a 2.2 to 8.62-fold increase in mortality compared with the patients of normal weight. A recent meta-analysis of twenty cohort studies evaluating 28,355 hospitalized patients reported a 1.5-fold increase in mortality [27]. Consistent with these previous reports, obesity but not being overweight, was an independent predictor of mortality in our study. Multivariate analysis in the present study revealed that the mortality rate increased 2.56-fold in obese and 3.88-fold in morbidly obese patients.

Obesity, diabetes, hypertension, CVD, heart failure, and chronic kidney disease have been observed to be the most common comorbidities in hospitalized patients with COVID-19. A study conducted in New York, USA reported that the prevalence of diabetes, hypertension, and obesity in COVID-19 patients were 33.8, 56.6, and 41.7 %, respectively [28]. In another meta-analysis including data of 38,906 COVID-19 patients and 77 studies, the prevalence of hypertension, diabetes, heart disease, and chronic kidney disease were 66, 38, 37, and 27 %, respectively [29]. Our findings were comparable with those reported in the above-mentioned studies. We observed a higher prevalence of comorbidities in our obesity group compared to patients in the normal weight group. Most, but not all, studies have reported that these comorbidities including diabetes, hypertension, chronic kidney disease, and CVD are predictors of worse outcomes and mortality [30–32]. A recent cohort in the USA of hospitalized patients with diabetes and COVID-19 showed that rather than long-term glycemic control, obesity was predictive of mortality. Likewise, CVD, chronic kidney disease, and COPD were all strongly predictive of mortality, while hypertension was even protective [33]. In our cohort study, age, male gender, pulmonary involvement on CT, chronic kidney disease, and high CRP levels were found to be independently associated with mortality, but after multivariate adjustment, we found that diabetes, hypertension, CVD were not associated with mortality in COVID-19 patients.

Several studies have shown that overweight and obese patients experience higher rates of hospitalization and ICU admission [7, 30]. In fact, hospitalization risk was found to increase even at modest weight gain [31]. Supporting these previous reports, higher hospitalization rates, longer hospital stays, and higher ICU admission rates in our cohort were observed in both overweight and obese patients compared to the normal-weight group. However, after multivariate adjustment, obesity or being overweight were not independent predictors of hospitalization. Our study was conducted when the first wave of COVID-19 infections occurred. The majority of patients preferred isolation and treatment in hospitals during the early pandemic for reasons like underdeveloped risk assessment methods, unknown disease course, limited isolation rooms, and pressure to hospitalize the confirmed cases for isolation purposes. Indeed, 48.8 % of inpatients in our dataset suggest an unbalanced promotion of hospitalization. All these confounding factors might affect the independent role of obesity in terms of the hospitalization rate in our study.

Studies showed that increased visceral fat and obesity are independently associated with the need for ICU admission and invasive mechanical ventilation in COVID-19 patients. However, most of these studies were carried in a relatively small number of patients [32, 33]. Our study highlighted that overweight and obese patients with COVID-19 required ICU and mechanical ventilation.

Even though females and males are equally infected by COVID-19, most studies reported higher mortality rates due to COVID-19 in men [34, 35], while another recent study suggested that obese women could be at a higher risk for mortality due to COVID-19 [36]. Sex-specific differences in genes encoding SARS-CoV2 entry receptors, the effect of sex hormones on immune response, and the association of more common risk factors in males may have a role in

▶ **Table 2** Multivariable logistic regression analysis of the patients diagnosed with new coronavirus disease 2019 (COVID-19) (dependent variable: intubation, hospitalization, mortality).

	Hospitalization		Intubation		Mortality	
	OR, 95 % CI	**p**	**OR, 95 % CI**	**p**	**OR, 95 % CI**	**p**
Age (years)	1.01, 1.01–1.02	**< 0.001**	1.04, 1.02–1.05	**< 0.001**	1.07, 1.06–1.09	**< 0.001**
Gender (male)	-	-	1.60, 1.11–2.30	**0.011**	2.45, 1.63–3.70	**< 0.001**
CRP, > ULN	-	-	2.25, 1.40–3.62	**0.001**	3.35, 1.82–6.17	**< 0.001**
CT findings of COVID-19	1.98, 1.59–2.47	**< 0.001**	1.80, 1.26–2.57	**0.001**	1.48, 1.01–2.17	**0.046**
Chronic kidney disease	-	-	1.96, 1.29–2.96	**0.001**	2.38, 1.56–3.65	**< 0.001**
Weight categories						
(Ref.: Normal weight)						
Overweight	–	–	1.82, 1.04–3.21	**0.037**		
Obesity	–	–	2.69, 1.51–4.76	**0.001**	2.56, 1.40–4.67	**0.002**
Morbid obesity	–	–	2.86, 1.08–7.59	**0.035**	3.88, 1.40–10.80	**0.009**

(CRP, C-reactive protein; ULN, upper limit of normal; CT, computerized tomography; COVID-19, coronavirus disease 2019 disease; OR, odds ratio; CI, confidence interval; Normal weight, BMI = 18.5–24.9 kg/m^2; Overweight, BMI = 25–29.9 kg/m^2; Obesity, BMI = 30–39.9 kg/m^2; Morbid obesity, BMI ≥ 40 kg/m^2). **Variables included in the model:** Age, gender, CRP, pulmonary CT findings of COVID-19, hypertension, type 2 diabetes mellitus, dyslipidemia, asthma/chronic obstructive pulmonary disease, chronic kidney disease, cardiovascular disease, cancer, and BMI (nonsignificant associations are not shown).

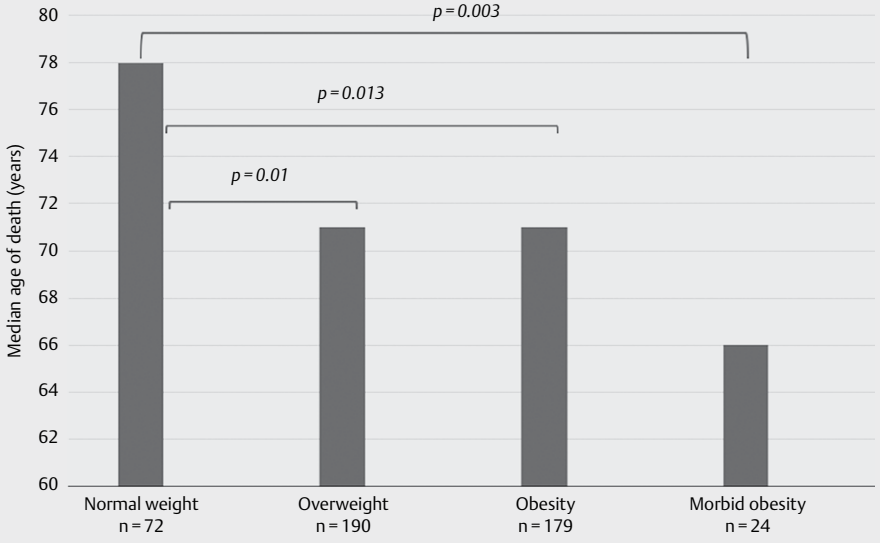
▶ **Table 3** Multivariable logistic regression analysis of the patients diagnosed with new coronavirus disease 2019 (COVID-19) according to the body mass index (BMI) categories (dependent variable: mortality).

	Normal weight		Overweight		Obesity	
	OR, 95 % CI	**p**	**OR, 95 % CI**	**p**	**OR, 95 % CI**	**p**
Age, years	1.11, 1.06–1.17	**< 0.001**	1.07 1.04–1.11	**< 0.001**	1.06 1.03–1.09	**< 0.001**
Gender (male)	-	**-**	2.49 1.21–5.14	**0.013**	2.53 1.45–4.41	**0.001**
Heart failure	-	**-**	2.49 1.08–5.70	**0.031**	-	**-**
Chronic kidney disease	-	**-**	2.17 1.05–4.48	**0.037**	3.88 2.11–7.16	**< 0.001**
Cancer	-	**-**	2.85 1.25–6.52	**0.013**	-	**-**
CRP, > ULN	-	**-**	3.05 1.11–8.35	**0.03**	3.36 1.45–7.79	**0.005**

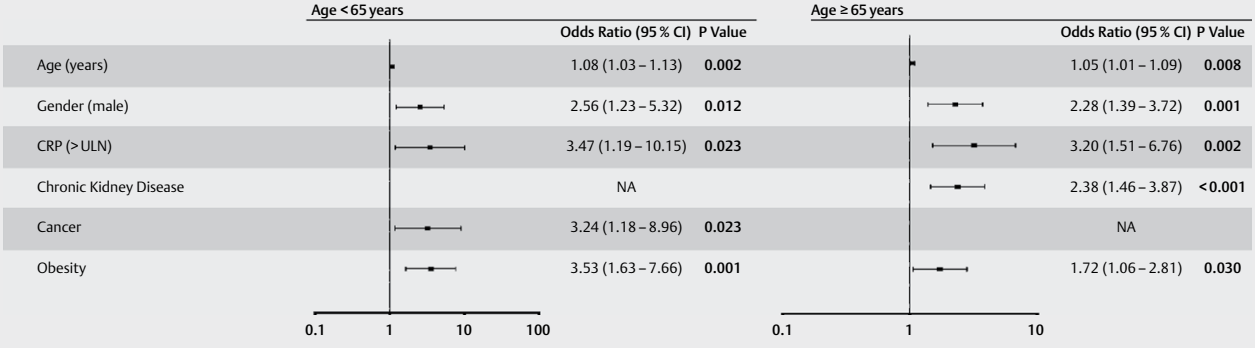
(CRP, C-reactive protein; ULN, upper limit of normal; OR, odds ratio; CI, confidence interval). **Variables included in the model**: Age, gender, CRP, pulmonary computerized tomography findings of coronavirus disease 2019, hypertension, dyslipidemia, type 2 diabetes mellitus, asthma/chronic obstructive pulmonary disease, heart failure, chronic kidney disease, cardiovascular disease, cancer, and obesity (nonsignificant associations are not shown).

the development of these adverse outcomes [37]. However, it is not clear whether the mortality risk in obesity is different between the males and females infected with COVID-19. In this regard, we evaluated the effect of obesity on mortality in male and female patients, separately and found that obesity independently and almost equally increased the mortality in both female and male patients (OR, 95 % CI: 2.21, 1.14–4.29; p = 0.019) vs. (OR, 95 % CI: 2.16, 1.28–3.64; p = 0.004), respectively.

Seventy-five percent of the total number of deaths are observed in patients aged 65 years or above in the COVID-19 pandemic. However, it has been suggested that the presence of obesity may shift the COVID-19 severity and associated mortality to younger patients [38–40]. Increased risk of in-hospital mortality and mechanical ventilation for adults < 35 years old with morbid obesity have been reported [41]. Another study reported a more robust relation between BMI and mortality in patients ≤ 60 years old compared to that in the older patients [42]. Recently, it was demonstrated that higher mortality risk in those with higher BMI is limited mostly to individuals ≤ 50 years old with morbid obesity [43]. According to the results of the present study, the median age of mortality in normal-weight patients (78 years) was significantly higher than that of the overweight (71 years), obese (71 years), and morbidly obese (66 years) patients. In our study, we compared data of patients below 65 years of age to those of 65 years and older. In both groups, obesity was independently associated with mortality but the effect of obesity on mortality was twice more in patients below



▶ **Fig. 2** Median age at death due to COVID-19 disease, across BMI categories.



▶ **Fig. 3** Forest plot graph of multivariable logistic regression analysis of patients across the age groups (dependent variable mortality).

65 years old. The reasons for the higher association of obesity with mortality in younger versus older patients are not clear; possibly, older patients with COVID-19 already have several other important confounding risk factors or comorbidities that affect the multivariate analysis.

Study limitations and strengths

Our study has a few limitations. First, it is a retrospective study based on the information provided in an electronic database, therefore, the possibility of unmeasured confounding factors should be taken into account. Measurements of some parameters like arterial blood pressures or oxygen saturation were not available in the database system. Second, the analysis was cross-sectional, therefore, a causal relationship between different BMI classes and mortality cannot be inferred from this study. Strengths of the study include the large sample size, wide representation of the population, and inclusion of confirmed COVID-19 with SARS-CoV-2 PCR test. Also, a similar protocol was followed to treat all patients under the guidance of the National Scientific Advisory Committee for COVID-19, resulting in a better standardization of patient care as well as limiting the treatment bias in our study.

The present study shows that patients who were overweight or obese were more likely to experience severe progression, adverse outcomes, and mortality during the course of COVID-19 infection. In addition to being overweight and obese, older age, male gender, chronic kidney disease, and high CRP levels were the main determinants of mortality. The risk of mortality associated with obesity was observed to be higher in patients less than 65 years old but it was similar among male and female COVID-19 patients. In conclusion, not only obese but also overweight patients are at risk for severe outcomes of COVID-19 disease. These patients should receive urgent medical attention and active treatment.

▶ **Table 4** Multivariable logistic regression analysis of the patients diagnosed with new coronavirus disease 2019 (COVID-19) according to gender (dependent variable: mortality)

	Female		Male	
	OR, 95% CI	**p**	**OR, 95% CI**	**p**
Age, years	1.08, 1.05–1.11	**<0.001**	1.07, 1.04–1.09	**<0.001**
CRP, >ULN	-	-	5.28, 2.04–13.64	**0.001**
COVID-19 findings on thorax CT	1.34, 0.73–2.46	**0.034**	1.53, 0.92–2.53	0.100
Chronic kidney disease	3.88, 1.98–7.59	**<0.001**	1.73, 0.99–3.03	0.054
Obesity	2.21, 1.14–4.29	**0.019**	2.16, 1.28–3.64	**0.004**

(CRP, C-reactive protein; ULN, upper limit of normal; CT, computerized tomography; COVID-19, new coronavirus disease 2019; OR, odds ratio; CI, confidence interval). **Variables included in the model**: Age, gender, CRP, pulmonary CT findings of COVID-19, hypertension, dyslipidemia, type 2 diabetes mellitus, asthma/chronic obstructive pulmonary disease, heart failure, chronic kidney disease, cardiovascular disease, cancer, and obesity (nonsignificant associations are not shown).

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Conflicts of interest

The authors have no potential conflicts of interest to disclose.

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