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Impact of obesity on COVID-19 patients

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ABSTRACT

With the increasing prevalence of obesity, there is a growing awareness of its impact on infectious diseases. In past epidemics of influenza A and Middle East respiratory syndrome (MERS) coronavirus, obesity has been identified as a risk factor influencing the severity of illness in infected persons. The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is responsible for a large number of deaths and health damages worldwide. Increasing numbers of reports have linked obesity to more severe COVID-19 disease and death. This review focuses on the impact of obesity on patients with COVID-19. We comprehensively analyzed the various mechanisms of obesity affecting the severity of the disease. In addition, on the basis of the vulnerability of people with obesity during the COVID-19 epidemic, we summarized both individual-level and hospital-level prevention and management measures for COVID-19 patients with obesity and discussed the impact of isolation on people with obesity.

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1. Introduction

Obesity is defined as abnormal or excessive fat accumulation that presents a risk to health. According to the World Health Organization (WHO) standards, one with a body mass index (BMI) $>30 \text{ kg/m}^2$ is classified as obese, which is also defined by a cutoff value of 28 kg/m^2 according to other standards in some countries such as China.¹ According to the State of Food Security and Nutrition in the World in 2019, obesity rates are increasing in almost every country in the world, with the global adult obesity rate reaching 13.2%,² placing a severe burden on families and society. Body overweight and obesity are well-established risk factors for chronic diseases including diabetes, and patients with diabetes and obesity were more likely to have diabetic complications than their counterparts without obesity.³ Achieving a healthy weight is considered a risk modifier and has a favorable effect on blood pressure, glucose metabolism, and cardiac and vascular function.

As the prevalence of obesity increases, people are becoming increasingly aware of its impact on infectious diseases. During the 2009 influenza A (H1N1) pandemic, obesity was identified for the first time as a risk factor for increased disease severity and increased mortality among infected individuals.⁴ The incidence of obesity among patients with MERS-CoV was about twice as high as that of patients with H1N1 ($7.7 \pm 2.8\%$), reaching $17.6 \pm 4.2\%$.⁵ In clinical studies of H1N1, obesity was linked to an increased risk for hospitalization,⁶ intensive care unit (ICU) admission,⁷ and invasive mechanical ventilation (IMV).⁸ Severe obesity (BMI $>40 \text{ kg/m}^2$) was associated with a twofold increased risk of death from H1N1 infection (OR = 2.01, 95% CI: 1.29–3.14).⁹ Furthermore, symptomatic adults with obesity were shown to shed the influenza A virus 42% longer than adults without obesity (adjusted event time ratio [ETR], 1.42; 95% CI: 1.06–1.89),¹⁰ making their exposure to viruses longer than their peers with normal weight.

Such disproportionate burdens may also exist among patients infected by the coronavirus disease 2019 (COVID-19), which have resulted in 39.5 million infections including 1.1 million deaths worldwide as of October 17, 2020, also causing massive damage to the global economy, education, and medical treatment. Although few systematic reviews have been conducted between COVID-19 and obesity, a meta-analysis of obesity and influenza-related pneumonia¹¹ showed that, compared with people with a normal BMI, the risk of pneumonia among individuals with obesity (BMI $\geq 30 \text{ kg/m}^2$) was increased 1.33 times (95% CI: 1.05–1.63), and 4.6 times (95% CI: 2.2–9.8) among individuals with morbid obesity (BMI $\geq 40 \text{ kg/m}^2$). Interestingly, the adult respiratory distress syndrome (ARDS) caused by severe lung infection has a high fatality rate, whereas patients with ARDS combined with obesity or morbid obesity have a lower mortality rate.¹² This paradox may be due to the fact that obesity-triggered low-grade inflammatory processes may constitute pre-conditioning insults or trigger anti-inflammatory adaptive mechanisms, thus providing a protective effect on ARDS.¹³ More research is needed to confirm this mechanism. We should also consider whether there is such a paradox in the impact of obesity on COVID-19.

A growing number of studies have tried to link obesity to COVID-19 severity and/or death.^{14–16} For example, preliminary epidemiological data from the US Centers for Disease Control and Prevention showed that among COVID-19 patients with obesity, 69% had a body mass index (BMI) between 30 and 40 kg/m^2 , and 30.1% had severe obesity (BMI $\geq 40 \text{ kg/m}^2$).¹⁷ Also, the obesity rate after sex and age standardization among 340 severe COVID-19 patients in France was significantly higher than that among the general French adult population.¹⁸ However, there have not been any comprehensive reviews on this association, which deserves to be systematically studied. This systematic review summarizes the epidemiological characteristics of (hospitalized or diagnosed) COVID-19 patients with obesity, where obesity is defined by the local BMI classification criteria. Then, the impact of obesity on the severity of COVID-19 in existing research is synthesized (Table 1), with

various mechanisms by which obesity may aggravate COVID-19 summarized. In addition, on the basis of the vulnerability of people with obesity during the COVID-19 epidemic, we summarize both individual-level and hospital-level management measures for COVID-19 patients with obesity. We also reviewed the impact of isolation on people with obesity and suggest additional prevention measures for this population.

2. Search strategy and study inclusion

A comprehensive literature review was conducted in the PubMed bibliography databases on October 1, 2020. We searched titles or abstracts including any combination of the keywords in two groups: 1) “COVID-19”, “COVID19”, “coronavirus disease 2019”, “2019 novel coronavirus disease”, “2019-nCoV”, “severe acute respiratory syndrome coronavirus 2”, “SARS-CoV-2”, and “SARS2”; and 2) “obesity”, “overweight”, “obese”, “adiposity”, “body mass index”, “BMI”, and “weight gain”. Titles and abstracts of the articles identified through the keyword search were independently screened by two reviewers against the study selection criteria: 1) study design: observational studies including cross-sectional and longitudinal studies; 2) study subject: COVID-19 patients with overweight or obesity, excluding pregnant women and children; 3) study outcome: COVID-19 severity, including hospital stays, IMV needing, ICU admission, death of COVID-19 patients; 4) article type: peer-reviewed publications that are not letters, comments, editorials, study/review protocols, review articles, animal studies, mechanistic studies, or case reports; and 5) language: English. Potentially relevant articles were retrieved for an evaluation of the full text by two independent reviewers with discrepancies resolved by a third reviewer. A total of 64 articles were finally included in this review after the whole filtering process (Fig. 1). The basic characteristics of the 63 included studies, including the prevalence of obesity and obesity-related COVID-19 progression, were summarized (Table 1).

3. Impact of obesity on COVID-19 severity

Age is one of the most important factors in the hospitalization rate of COVID-19, with about 70% of the hospitalized cases aged over 45.^{19,20} Obesity, as the most common underlying condition for patients with COVID-19 aged under 64 years old,¹⁷ could shift the COVID-19 risk to younger ages.^{19,20} Obesity can also increase the risk factors for these diseases and lead to unfavorable consequences. The clinical spectrum of COVID-19 is very broad, and the common symptoms of most patients with COVID-19 are non-specific, including fever (98%), cough (76%), and myalgia or fatigue (44%).²¹ For patients with comorbidities, COVID-19 may bring about acute respiratory illnesses, respiratory failure, and septic shock, and in the most severe cases, ARDS.²² By studying the relationship between the severity of COVID-19 and obesity, we can deploy medical resources in the most cost-effective manner to prevent health systems from overloading and focus on the most fragile cohort of patients during all phases of the disease.²³

3.1. Effects of obesity on recovery time of COVID-19 patients

The recovery of patients with COVID-19 represents the gradual regression of clinical symptoms and signs of the body. The time taken for recovery is not only closely related to the severity of COVID-19²⁴ but also influences the spread of the virus and the additional economic burden,²⁵ in which obesity may play a role. In a small sample ($n = 34$) study²⁶ in Israel, the researchers used negative results from two of three genes (envelope protein gene (E), RNA-dependent RNA polymerase gene (RdRP), and nucleocapsid (N) gene) measured by RT-PCR as criteria for patient recovery. Patients with obesity had a higher mean length of hospital stay than patients without obesity (20.6 vs 16.0 days), suggesting that the recovery time of COVID-19 patients with obesity may be different from that of normal-weight patients, with longer

Table 1
The prevalence and prognosis of COVID-19 with obesity.

First author (year)	Study design	Subject	Number of participants	Country	Age (median)	Males (%)	Prevalence of COVID-19 with obesity	Prognosis of COVID-19 with obesity	Complications of COVID-19
Anderson (2020) ¹⁰⁷	Cross-sectional study	Hospitalized	2673	USA	67 (median)	58	NA	Obesity was association with higher risk for adverse outcome (intubation or death) among patients younger than 65 years.	Comorbidities: hypertension (50%) and diabetes (19%)
Biscarini (2020) ¹⁰⁸	Cohort study	Hospitalized	331	Italy	67 (mean)	68.2	24%	The association between obesity and the ICU admission of COVID-19 was statistically significant (OR = 1.96, 95% CI 1.03–3.75).	Comorbidities: hypertension (52%) and diabetes (40%)
Deng (2020) ¹⁰⁹	Cohort study	Hospitalized	65	China	NA	NA	NA	The severe/critical cases of BMI ≥28 kg/m ² patients were more than BMI ≤24 kg/m ² patients (<i>p</i> < 0.001).	NA
Docherty (2020) ⁴⁸	Cohort study	Hospitalized	20,133	UK	72.9 (median)	59.9	10.5% (1685/16081)	The association between obesity and the death of COVID-19 was statistically significant (OR = 1.33, 95% CI 1.19–1.49 (<i>p</i> < 0.001)).	Comorbidities: diabetes without complications (33.7%) and chronic cardiac disease (30.9%) The association between chronic cardiac disease and the death of COVID-19 was statistically significant (OR = 1.16, 95% CI 1.08–1.24 (<i>p</i> < 0.001)). Comorbidities: hypertension (70%), pre-existing respiratory disease (50%) and diabetes (58%)
Dreher (2020) ⁵¹	Cohort study	Hospitalized	50	Germany	65 (median)	66	34%	COVID-19 with obesity patients had a higher incidence of ARDS than non-obesity patients (46%/23%).	Comorbidities: diabetes (19.3%)
Gao (2020) ²⁷	Cohort study	Hospitalized	150	China	48 (median)	62.7	50% (randomized trial, obesity/non-obesity = 1:1)	COVID-19 with obesity patients were more severe than non-obesity patients (33.3%/14.7%, <i>p</i> = 0.007). COVID-19 with obesity patients had a longer hospital stays than non-obesity patients (median 23 (IQR 17–30)/18 (13–24) days, <i>p</i> = 0.037).	NA
Giacomelli (2020) ⁴⁷	Cohort study	Hospitalized	233	Italy	61 (median)	69.1	NA	The association between obesity and the death of COVID-19 was statistically significant (aHR = 3.04, 95% CI 1.42–6.49).	NA
Gupta (2020) ¹¹⁰	Cohort study	Hospitalized	2215	USA	60.5 (mean)	64.8	NA	The ICU admission of BMI >40 kg/m ² patients were higher than BMI >25 kg/m ² patients (OR = 1.51, 95% CI: 1.01–2.25).	NA
Hu (2020) ³¹	Cohort study	Hospitalized	323	China	61 (median)	51.4	4%	The proportion of BMI >25 kg/m ² in critical group was higher than that in general group (23.1%/20.7%).	NA
Jakob (2020) ¹¹¹	Cohort study	Hospitalized	2155	European (112 countries)	NA	59.7	NA	The complicated clinical stage of BMI >35 kg/m ² patients were higher than 18.5 < BMI <24.9 kg/m ² patients (OR = 2.21, 95% CI: 1.43–3.43).	Comorbidities: diabetes mellitus (18.4%) and CVD (55.7%) The association between diabetes mellitus and the complicated clinical stage of COVID-19 was statistically significant (aOR = 1.33, 95% CI 1.04–1.69).
Nakeshbandi (2020) ¹¹²	Cohort stud	Hospitalized	504	USA	68 (median)	52	43%	Overweight (RR = 1.4, 95% CI 1.1–1.9) and obesity (RR = 1.3, 95% CI 1.0–1.7) was significantly increased risk of mortality of COVID-19. Overweight (RR = 2.0, 95% CI 1.2–3.3) and obesity (RR = 2.4, 95% CI 1.5–4.0) was significantly increased risk of intubation of COVID-19.	The association between CVD and the complicated clinical stage of COVID-19 was statistically significant (aOR = 1.37, 95% CI 1.09–1.72). Comorbidities: diabetes (53%) and hypertension (83%)
Nguyen (2020) ¹¹³	Cohort study	Hospitalized	279	France	64.8 (mean)	65.6	20.4%	The risk of IMV needing and death of BMI ≥25 kg/m ² patients were higher than BMI <25 kg/m ² patients (aHR = 2.14, 95% CI: 1.32–3.47 (<i>p</i> = 0.002)).	Comorbidities: diabetes (27.6%), hypertension (47.0%) and coronary heart disease (10.8%)
Ortiz-Brizuela (2020) ²⁹	Cohort study	Diagnosed	309	Mexico	43 (median)	59.2	39.6%	ICU patients had a higher BMI than non-ICU patients (BMI, median 30.5 vs 28.7).	NA
Pettit (2020) ¹¹⁴	Cohort study	Hospitalized	238	USA	58.5 (mean)	37.5	61.3%	The mortality of COVID-19 patients in obesity group was higher than that in non-obesity group (OR =	Comorbidities: diabetes (28.6%) and hypertension (52.9%)

(continued on next page)

Table 1 (continued)

First author (year)	Study design	Subject	Number of participants	Country	Age (mean)	Males (%)	Prevalence of COVID-19 with obesity	Prognosis of COVID-19 with obesity	Complications of COVID-19
Rottoli (2020) ¹¹⁵	Cohort study	Hospitalized	482	Italy	NA	NA	21.6%	1.7, 95% CI 1.1–2.8 ($p = 0.016$). The risk of respiratory failure (OR = 2.32, 95% CI: 1.31–4.09 ($p = 0.004$)) and ICU admission (OR = 4.96, 95% CI: 2.53–9.74 ($p < 0.001$)) of 30 \leq BMI <35 kg/m ² patients were higher than BMI <30 kg/m ² patients.	NA
Simonnet (2020) ⁴³	Cohort study	Hospitalized	124	France	60 (median)	73	47.5%	The risk of death of BMI \geq 35 kg/m ² patients were higher than BMI <30 kg/m ² patients (OR = 12.1, 95% CI: 3.25–45.1 ($p < 0.001$)). The IMV needing of BMI >35 kg/m ² patients were higher than BMI >25 kg/m ² patients (OR = 7.36, 95% CI: 1.63–33.14 ($p = 0.02$)). IMV requirement increased with BMI ($p < 0.01$, chi-square test).	Comorbidities: diabetes (23%), hypertension (49%), dyslipidemia (28%)
Tartof (2020) ¹¹⁶	Cohort study	Diagnosed	6916	USA	49.1 (mean)	45.0	NA	The risk of death of BMI \geq 45 kg/m ² patients were higher than normal BMI (18.5–24 kg/m ²) patients (OR = 4.18, 95% CI: 3.25–45.1 ($p < 0.001$)).	NA
Yanover (2020) ¹¹⁷	Cohort study	Hospitalized	4353	Israel	NA	55.5	20.1%	Obesity for patients younger than 65 years was significantly association with higher risk for severe symptoms (OR = 3.4, 95% CI: 1.88–6.14 ($p = 0.001$)).	Diabetes (OR = 3.16, 95% CI: 1.32–6.79 ($p = 0.04$)), CVD (OR = 2.76, 95% CI: 1.88–6.14 ($p = 0.001$)) and hypertension (OR = 4.56, 95% CI: 1.29–5.85 ($p = 0.045$)) for patients 18–50 years old was significantly association with higher risk for severe symptoms. Comorbidities: diabetes mellitus (48.1%), hypertension (67.7%)
Alkhatib (2020) ¹¹⁸	Cross-sectional study	Hospitalized	158	USA	57 (mean)	38.6	NA	Patients admitted to the ICU had higher BMI (26.5 kg/m ² /31.9 kg/m ² , $p = 0.002$).	Diabetes (OR = 3.16, 95% CI: 1.32–6.79 ($p = 0.04$)), CVD (OR = 2.76, 95% CI: 1.88–6.14 ($p = 0.001$)) and hypertension (OR = 4.56, 95% CI: 1.29–5.85 ($p = 0.045$)) for patients 18–50 years old was significantly association with higher risk for severe symptoms. Comorbidities: diabetes mellitus (48.1%), hypertension (67.7%)
Bello-Chavolla (2020) ¹¹⁹	Cross-sectional study	Diagnosed	51,633	Mexico	46.5 (mean)	57.7	20.7%	The association between obesity and the risk of death in COVID-19 patients was statistically significant (HR = 1.25, 95% CI 1.17–1.34, ($p < 0.001$)).	Comorbidities: diabetes (18.3%), hypertension (21.6%)
Busetto (2020) ⁶⁴	Cross-sectional study	Hospitalized	92	Italy	NA	61.9	65.2%	The IMV needing of overweight (16.1%) or obesity (6.9) patients were higher than normal weight (6.2%) patients. The assisted ventilation (NIV and IMV) needing of overweight (54.8%) or obesity (41.4%) patients were higher than normal weight (15.6%) patients.	The association between diabetes and the risk of death in COVID-19 patients was statistically significant (HR = 1.34, 95% CI 1.26–1.43, ($p < 0.001$)).
Cai (2020) ⁵⁵	Cross-sectional study	Hospitalized	96	China	NA	NA	NA	BMI was higher in COVID-19 patients with pneumonia than in those without pneumonia (23.81 kg/m ² /20.78 kg/m ² , $p = 0.001$).	Comorbidities: diabetes (30.4%) and respiratory chronic disease (13.0%)
Cai (2020) ¹²⁰	Cross-sectional study	Hospitalized	383	China	NA	47.8	10.7%	Severe cases in normal weight group/overweight group/obesity group: 19.2%/29.3%/39.0% ($p = 0.001$).	Comorbidities: diabetes (5.7%), hypertension (15.1%) and CVD (9.1%)
Carou (2020) ¹²¹	Cross-sectional study	Hospitalized and diabetic	1317	France	69.8 (mean)	64.9	38.3%	The association between BMI and the primary outcome (tracheal intubation and/or death within 7 days of admission) was statistically significant ($p < 0.001$).	The proportion of hypertension in severe group was higher than that in non-severe group (23.08%/12.67% ($p = 0.02$)).
Caussy (2020) ¹⁸	Cross-sectional study	Hospitalized and severe	340	Italy	NA	NA	25%	The proportion of obesity in severe COVID-19 patients was higher than that in general French adult population (OR = 1.35, 95% CI: 1.08–1.66). The proportion of obesity in critical COVID-19	The proportion of CVD in severe group was higher than that in non-severe group (18.68%/6.16% ($p = 0.001$)). Comorbidities: hypertension (77.2%) The association between hypertension and death of COVID-19 was statistically significant (OR = 1.82, 95% CI: 1.11–2.98). NA

Table 1 (continued)

First author (year)	Study design	Subject	Number of participants	Country	Age	Males (%)	Prevalence of COVID-19 with obesity	Prognosis of COVID-19 with obesity	Complications of COVID-19
Hur (2020) ¹²⁸	Cross-sectional study	Hospitalized	486	USA	58 (median)	55.8	53.3%	The extubation chance of BMI <30 kg/m ² intubated patients were higher than 30 < BMI <39.9 kg/m ² patients (OR = 0.53, 95% CI: 0.32–0.90) or BMI ≥40 kg/m ² patients (OR = 0.40, 95% CI: 0.19–0.82). COVID-19 with obesity patients had a higher IMV needing than non-obesity patients (OR = 2.6, 95% CI: 1.05–44.82).	ICU admission of COVID-19 patients with complication: 5.4% NA
Kalligeros (2020) ³⁴	Cross-sectional study	Hospitalized	103	USA	60 (median)	61.1	47.5%		Comorbidities: hypertension (64.0%), heart disease (24.2%), and diabetes (36.8%) ICU admission of COVID-19 patients with complication: 39.8% NA
Kass (2020) ¹⁹	Cross-sectional study	Hospitalized	265	USA	NA	58	NA	The negative association between BMI and age was significant ($r^2 = 0.051, p = 0.0002$).	NA
Kim (2020) ¹²⁹	Cross-sectional study	Hospitalized	2491	USA	62 (median)	53.2	49.7%	The association between obesity and the risk of ICU admission in COVID-19 patients was statistically significant (aRR = 1.31, 95% CI 1.16–1.47).	Comorbidities: hypertension (57.4%), CVD (34.6%) and diabetes (32.9%) The association between diabetes and the risk of ICU admission in COVID-19 patients was statistically significant (aRR = 1.13, 95% CI 1.03–1.24). NA
Klang (2020) ¹³⁰	Cross-sectional study	Hospitalized	3406	USA	NA	57.6	36.1%	At age < 50, BMI >40 was independently associated with mortality (OR = 5.1, 95% CI 2.3–11.1). At age > 50, BMI >40 was independently associated with mortality (OR = 1.6, 95% CI 1.2–2.3).	NA
Ko (2020) ²⁰	Cross-sectional study	Hospitalized	5416	USA	NA	NA	55%	The association between obesity (aRR = 2.9, 95% CI 2.3–3.5) or severe obesity (aRR = 4.4, 95% CI 3.4–5.7) and the risk of COVID-19-associated hospitalization was statistically significant.	Comorbidities: hypertension (49%) and diabetes (33%) The association between hypertension (aRR = 3.6, 95% CI 2.3–5.8) or diabetes (aRR = 3.2, 95% CI 2.5–4.1) and the risk of COVID-19-associated hospitalization was statistically significant NA
Lighter (2020) ³³	Cross-sectional study	Hospitalized	3615	USA	NA	NA	37.9%	At age < 60, the critical care needing of BMI ≥30 kg/m ² patients were higher than BMI <30 kg/m ² patients (OR = 1.8, 95% CI: 1.2–2.7 ($p = 0.006$)). At age < 60, the critical care needing of BMI >35 kg/m ² patients were higher than BMI <30 kg/m ² patients (OR = 3.6, 95% CI: 2.5–5.3 ($p < 0.0001$)). The association between obesity and the risk of hospitalization in COVID-19 patients was statistically significant (aOR = 1.8, 95% CI 1.4–2.4, ($p < 0.0005$)). COVID-19 with obesity patients had a longer hospital stay than non-obesity patients ($21 \pm 8/13 \pm 8$ days, $p = 0.0008$).	NA
Imam (2020) ³⁰	Cross-sectional study	Diagnosed	2040	USA	NA	NA	NA		NA
Moriconi (2020) ²⁸	Cross-sectional study	Hospitalized	100	Italy	NA	52	29%	COVID-19 with obesity patients had a longer hospital stay than non-obesity patients ($21 \pm 8/13 \pm 8$ days, $p = 0.0008$).	Comorbidities: hypertension (55%), chronic heart failure (28%) and diabetes (25%)
Mughal (2020) ¹³¹	Cross-sectional study	Hospitalized	129	USA	63.0 (median)	62.8	14%	The proportion of obesity in IMV COVID-19 patients was higher than that in non-IMV COVID-19 patients (IMV/non-IMV = 26.7%/10.1% ($p = 0.0334$)).	Comorbidities: hypertension (43.4%) and diabetes mellitus (19.4%) The proportion of diabetes mellitus in IMV COVID-19 patients was higher than that in non-IMV COVID-19 patients (IMV/non-IMV = 36.7%/14.1% ($p = 0.0063$)). NA
Muñoz-Price (2020) ⁶⁷	Cross-sectional study	Hospitalized	2595	USA	53.8 (mean)	37.7	NA	The association between BMI and the risk of IMV (OR = 1.06, 95% CI 1.02–1.09, ($p = 0.003$)) and in-hospital death (OR = 1.19, 95% CI 1.05–1.35, ($p = 0.006$)) in COVID-19 patients was statistically significant.	NA
Onder (2020) ¹³²	Cross-sectional study	dead	3694	Italy	NA	NA	NA	The association between obesity and the risk of acute renal failure (OR = 1.33, 95% CI 1.04–1.71, ($p < 0.001$)) and shock (OR = 1.54, 95% CI 1.19–1.99, ($p < 0.001$)) in COVID-19 patients was statistically significant.	NA

Ong (2020) ⁴⁴	Cross-sectional study	Hospitalized	182	Singapore	NA	NA	NA	At age < 60, the IMV needing of BMI ≥ 25 kg/m ² patients were higher than BMI <25 kg/m ² patients (OR = 1.16, 95% CI: 1.00–1.34 ($p = 0.049$)). The mortality of COVID-19 patients varied significantly among BMI <25 kg/m ² group, BMI 25–34 kg/m ² group, BMI ≥ 35 kg/m ² group (31.6%/17.2%/34.8%, $p = 0.030$). The intubation of COVID-19 patients varied significantly among BMI <25 kg/m ² group, BMI 25–34 kg/m ² group, BMI ≥ 35 kg/m ² group (18.4%/16.4%/34.8%, $p = 0.032$). Both men (aHR = 1.78, 95% CI 1.44–2.21) and women (aHR = 2.21, 95% CI 1.69–2.88) with a higher BMI had a higher risk of death than those with a healthy weight.	NA	Comorbidities: hypertension (76%), hyperlipidemia (46.2%), and diabetes (39.5%)
Palaiodimos (2020) ⁴⁶	Cross-sectional study	Hospitalized	200	USA	64 (median)	49	NA	The association between BMI ≥ 35 kg/m ² and the risk of death in COVID-19 patients was statistically significant (aOR = 1.53, 95% CI 1.21–1.94).	NA	
Peters (2020) ¹³³	Cross-sectional study	Dead	410	UK	NA	64%	NA	The association between obesity and the risk of IMV (OR = 2.13, 95% CI 1.14–4.00) and ICU admission (OR = 2.16, 95% CI 1.20–3.88) in COVID-19 patients was statistically significant.	NA	
Rapp (2020) ¹³⁴	Cross-sectional study	Hospitalized	4062	USA	NA	57.4	NA	The association between morbid obesity and in-hospital mortality in COVID-19 patients was statistically significant (OR = 2.29, 95% CI 1.11–4.69 ($p = 0.02$)).	NA	
Seiglie (2020) ¹³⁵	Cross-sectional study	Hospitalized	450	USA	NA	NA	NA	The association between obesity and the risk of IMV hospitalization in COVID-19 patients was statistically significant (aOR = 1.74, 95% CI 1.35–2.23 ($p < 0.001$)).	NA	Comorbidities: diabetes (39.6%) The association between diabetes and the risk of IMV (OR = 1.97, 95% CI 1.21–3.20), death (OR = 2.13, 95% CI 1.14–4.00) and ICU admission (OR = 1.59, 95% CI 1.01–2.52) in COVID-19 patients was statistically significant.
Shah (2020) ¹³⁶	Cross-sectional study	Hospitalized	552	USA	63 (median)	42	66.5%	The association between severe obesity and the risk of IMV in COVID-19 patients was statistically significant (aOR = 4.5, 95% CI 1.98–10.27 ($p = 0.0003$)).	NA	Comorbidities: hypertension (79.7%) and diabetes mellitus (42.3%) The association between hypertension and in-hospital mortality in COVID-19 patients was statistically significant (OR = 3.36, 95% CI 1.3–8.6 ($p = 0.01$)).
Soares (2020) ⁵²	Cross-sectional study	Diagnosed	24,428	Brazil	NA	NA	NA	The association between obesity and the risk of hospitalization in COVID-19 patients was statistically significant (aOR = 1.10–1.61 ($p = 0.003$)) or CVD (aOR = 1.30, 95% CI 1.11–1.53 ($p = 0.001$)) and the risk of hospitalization in COVID-19 patients was statistically significant.	NA	The association between diabetes mellitus and the risk of IMV in COVID-19 patients was statistically significant (aOR = 1.34, 95% CI 1.10–1.61 ($p = 0.003$)) or CVD (aOR = 1.30, 95% CI 1.11–1.53 ($p = 0.001$)) and the risk of hospitalization in COVID-19 patients was statistically significant.
Sterling (2020) ¹³⁷	Cross-sectional study	Hospitalized	256	USA	NA	NA	NA	The association between severe obesity and the risk of IMV in COVID-19 patients was statistically significant (aOR = 3.2, 95% CI 1.7–6.0 ($p < 0.001$)).	NA	The association between history of diabetes mellitus and the risk of IMV in COVID-19 patients was statistically significant (aOR = 2.55, 95% CI 1.13–5.75 ($p = 0.023$)).
Suleyman (2020) ¹³⁸	Cross-sectional study	Diagnosed	463	USA	57.5 (mean)	44.1	57.2%	The association between severe obesity and the risk of IMV in COVID-19 patients was statistically significant (aOR = 5.000, 95% CI 1.611–15.516 ($p = 0.005$)) and obesity (OR = 11.333, 95% CI 3.329–38.583 ($p < 0.001$)) was significantly associated with severe illness of COVID-19.	NA	Comorbidities: hypertension (68.7%) and diabetes (38.8%)
Targher (2020) ¹³⁹	Cross-sectional study	Hospitalized	339	China	NA	NA	38.4%	The proportion of COVID-19 patients developing ARDS was higher in patients with obesity than lean patients (5.00%/0%, $p = 0.024$).	NA	
Wang (2020) ⁵⁶	Cross-sectional study	Hospitalized	297	China	38.00 (mean)	55.22	13.47%	The association between obesity and the risk of IMV (aOR = 2.36, 95% CI 1.33–3.20), ARDS (aOR = 2.44, 95% CI 1.28–4.65) and ICU admission (aOR = 2.18, 95% CI 1.25–3.81) in COVID-19 patients was statistically significant.	NA	Type 2 diabetes was significantly associated with severe illness of COVID-19 (OR = 5.333, 95% CI 1.800–15.800 ($p = 0.003$)).
Xie (2020) ¹⁴⁰	Cross-sectional study	Hospitalized	267	USA	61.5 (mean)	43.2	NA	The association between obesity and the risk of IMV (aOR = 2.12, 95% CI 1.16–3.89) and ICU admission (aOR = 2.22, 95% CI 1.24–3.98) in COVID-19 patients was statistically significant.	NA	The association between diabetes and the risk of IMV (aOR = 2.12, 95% CI 1.16–3.89) and ICU admission (aOR = 2.22, 95% CI 1.24–3.98) in COVID-19 patients was statistically significant.
Yu (2020) ⁵³	Cross-sectional study	Hospitalized	95	China	NA	NA	NA	The association between high BMI and the risk of pneumonia in COVID-19 patients was statistically significant (OR = 1.327, $p = 0.024$).	NA	

(continued on next page)

Table 1 (continued)

First author (year)	Study design	Subject	Number of participants	Country	Age (median)	Males (%)	Prevalence of COVID-19 with obesity	Prognosis of COVID-19 with obesity	Complications of COVID-19
Zheng (2020) ¹⁴¹	Cross-sectional study	Hospitalized and MAFLD	66	China	47.0 (median)	74.2	68.2%	COVID-19 with obesity patients were more severe than non-obesity patients (OR = 6.32, 95% CI: 1.16–34.54 (p = 0.033)).	NA

ARDS – acute respiratory distress syndrome; BMI – body mass index; CI – confidence interval; CVD – cardiovascular disease; GPU – general practice unit; ICU – intensive care unit; NIV – non-invasive mechanical ventilation; IMV – invasive mechanical ventilation; aHR – adjusted hazard ratio; aOR – adjusted odds ratio; NA – not available; NAFLD – nonalcoholic fatty liver disease; OR – odds ratio; RR – relative ratio.

discharge time. It also proves from another perspective that patients with obesity have a higher viral load and a slower antiviral response, thus affecting the disease progression of COVID-19.²⁶ Stronger evidence came from a paired cohort study in Wenzhou, China. In a group of 75 randomly matched patients by age and sex, the analysis found that patients with obesity had significantly longer hospital stays (23 vs 18 days, $p = 0.037$) and a higher proportion of severe COVID-19 (33.3% vs. 14.7%, $p = 0.007$) than patients without obesity, with a clear dose-effect.²⁷ The extension was even more pronounced in another study in Italy (21 ± 8 vs 13 ± 8 days, $p = 0.0008$).²⁸

3.2. Effects of obesity on ICU admission of COVID-19 patients

The ICU is a special department that provides intensive treatment medicine in hospitals or health care institutions. Most of the patients treated in ICUs are experiencing or recovering from life-threatening situations. BMI of patients with COVID-19 was significantly correlated with ICU treatment.^{29,30} A study in Hubei Province of China ($n = 323$) showed that patients with a BMI >25 kg/m² accounted for 22.1% of 172 severe and critically ill COVID-19 patients.³¹ Some scholars have suggested that the high obesity rates among intensive care patients infected with SARS-CoV-2 may depend on the local obesity rate.³² However, in a series of 3615 patients with COVID-19 from New York, US, those under 60 years of age with a BMI ranging from 30 to 34 kg/m² had a 1.8-fold increase in the probability of ICU admission compared to patients with a BMI <30 kg/m². This likelihood increased to 3.6-fold among patients with a BMI ≥ 35 kg/m².³³ Moreover, COVID-19 patients in ICUs had higher BMI than non-ICU patients (BMI, median 30.5 kg/m² vs 28.77 kg/m²). Interestingly, among the published proportion of patients admitted to the ICU during hospitalization in various countries, the proportion of patients transferred to the ICU in countries with high obesity rates, such as the United States (39.8%)³⁴ and Italy (19%)³⁵ was significantly higher than that in China (5.4%, non-Hubei region)³⁶ and South Korea (13.3%),³⁷ which have low obesity rates. Considering that this may be due to differences in health technology and varying degrees of aging, we need to attach significance to the role of obesity in the severe forms of COVID-19. This is probably caused by chronic diseases associated with obesity. Among 1591 patients treated in the ICU for COVID-19 patients in Lombardy, Italy, 68% (95% CI, 65%–71%) of the patients had at least one comorbidity, including hypertension (49%), cardiovascular diseases (21%), hypercholesterolemia (18%), and diabetes (17%),³⁸ all of which have been linked to obesity in previous studies.^{39–41}

3.3. Effects of obesity on IMV needing of COVID-19 patients

IMV is a means of life support, which is usually reserved as the last option for chronic obstructive pulmonary disease (COPD), which represents that patient's condition has entered a serious stage.⁴² There has been a significant association between obesity and IMV.^{43,44} For example, among 393 patients in New York City, patients who received IMV had a higher obesity rate than those who did not (43.4% vs 31.9%).⁴⁵ Likewise, in a retrospective cohort study in France, 124 patients with severe COVID-19 were analyzed, and IMV was used as a criterion to determine the severity of the disease. The results showed that the requirement of IMV significantly correlated with BMI ($p < 0.05$); the proportion of patients who required IMV increased with BMI categories ($p < 0.01$, chi-square test), and it was the greatest among patients with a BMI >35 kg/m² (85.7%). Additionally, BMI >35 kg/m² can increase the risk of IMV 7-fold and is associated with lower survival rates.⁴³ The same results were found in Ong's⁴⁴ and Palaiodimos's⁴⁶ studies. These studies demonstrated that obesity increases the risk of IMV among patients with COVID-19.

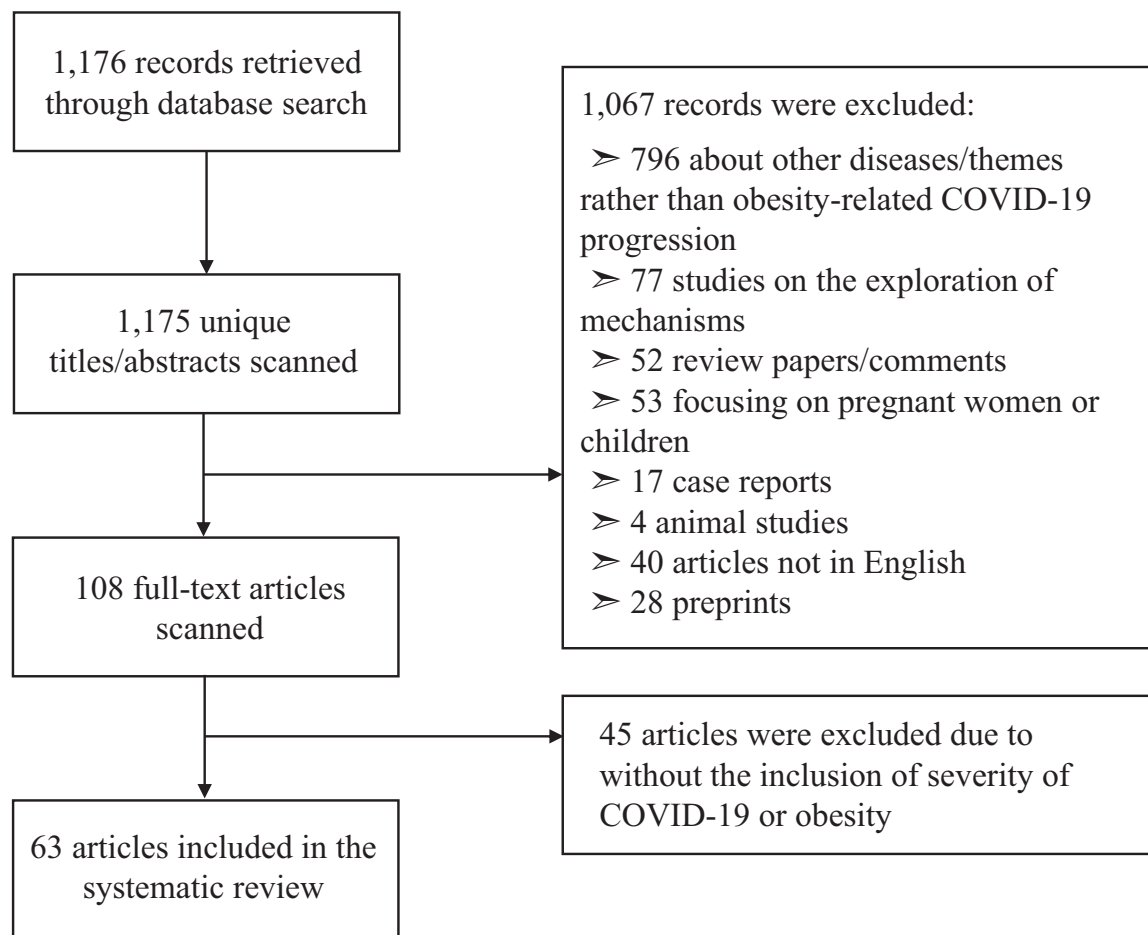


Fig. 1. Study exclusion and inclusion flowchart.

3.4. Effects of obesity on death of COVID-19 patients

Obesity has also been associated with an increased risk of death in hospitalized patients with COVID-19.^{47,48} In a cohort study in the Bronx, New York, it was found that severe obesity was independently associated with higher inpatient mortality and overall poor inpatient outcomes.⁴⁶ Similarly, a study in Milan, Italy found that 48 out of 233 hospitalized patients with COVID-19 who died had a significantly higher prevalence of obesity than those who survived (27.1% vs 13.5%, $p = 0.029$).⁴⁷ In addition, obesity has also been increasingly common even in persons younger than 50 years old relative to other known risk factors (e.g., hypertension, cardiovascular, Type 2 diabetes), and this high prevalence predicted a shift in severe COVID-19 disease, such as the risk of death, to younger populations.¹⁹ A retrospective study in New York that included 3406 hospitalized patients with COVID-19 found that younger patients with a BMI over 40 kg/m² were 5 times more likely to die.⁴⁹

3.5. Effects of obesity on other severity outcomes of COVID-19 patients

Obesity has also been associated with other COVID-19 severity outcomes.^{50–53} For example, among 212,802 patients diagnosed with COVID-19 in Mexico, obesity increased the risk of hospital admission by 1.29-fold ($p < 0.001$).⁵⁴ The BMI of patients with COVID-19 and pneumonia, a localized inflammation of the lungs, was significantly higher than those without pneumonia (23.81 vs 20.78 kg/m², $p = 0.001$).⁵⁵ Also, obesity increased the risk of pneumonia by 1.327-fold ($p = 0.024$).⁵³ ARDS leads to acute diffuse lung injury and subsequent

acute respiratory failure, characterized by respiratory distress and hypoxemia, and is almost one of the most severe consequences of COVID-19. The results of this study showed that the incidence of ARDS is significantly higher in the group with obesity compared to the lean group (5.00% vs 0%, $p = 0.024$).⁵⁶

The above content systematically summarizes the impact of obesity on the severity of COVID-19. Although most studies employed multivariate analysis to adjust the impact of obesity-related diseases (i.e., diabetes, hypertension and CVD) on the severity of COVID-19, making the role of obesity independent, we should not neglect the equal importance impact of obesity-related diseases due to the long-term accumulating effects on patients' physiology and psychology.⁵⁷ Among the 44,672 confirmed COVID-19 cases in China, the case fatality rate (CFR) was 2.3%, and 7.3% of the deaths (1023) were patients with diabetes, 10.5% were patients with cardiovascular disease, and 6.0% were patients with hypertension.⁵⁸ This suggests that we should give attention not only to obesity, but also to the impact of obesity-related diseases on COVID-19.

4. Mechanisms connecting obesity to COVID-19 severity

Obesity would likely increase the severity of COVID-19 since SARS-CoV-2 is transmitted by droplets or contact. The first line of defense (skin and nasal mucosa) and the second line of defense (bactericidal substances and phagocytes) of an immunocompromised individual cannot prevent and destroy the virus, which enters the lungs through the respiratory tract. Spike protein binds to the angiotensin-converting enzyme 2 (ACE2) receptor on lung cells to enter the cell, where it replicates, assembles, and releases a large number of viruses (Fig. 2). After the virus is phagocytized by alveolar epithelial macrophages, the target

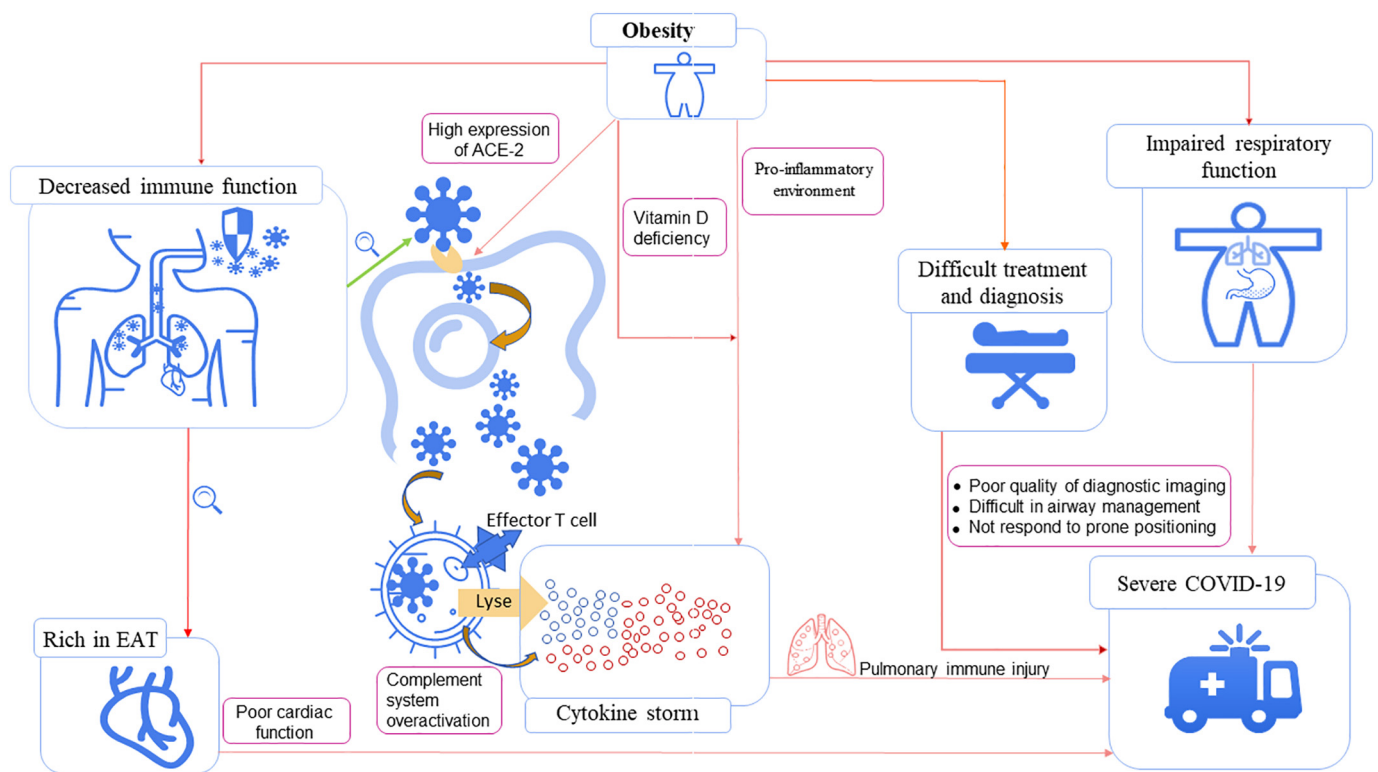


Fig. 2. Mechanisms connecting obesity to COVID-19 severity.

cells are lysed and killed by immune T cells through cellular immunity, and a large number of cytokines and complements are released. This autoinflammatory response leads to the destruction of lung cells, preventing the pulmonary alveoli from carrying out the normal blood oxygen exchange, inducing a series of clinical symptoms in patients. A large release of cytokines may lead to cytokine storms, and an excessive immune response may lead to a rapid decline in lung function, respiratory failure, viremia, ARDS and even multiple organ dysfunction syndrome (MODS).

4.1. Respiratory function

Obesity has detrimental effects on respiratory mechanics, the respiratory drive, and the physiology and anatomy of the upper respiratory function, directly affecting the respiratory function of patients with obesity.⁵⁹ Obesity leads to increased airway resistance, decreased respiratory muscle, reduced lung volume, and impaired gas exchange in patients. However, since SARS-CoV-2 is a virus that mainly attacks the respiratory system, patients' obesity status will further impair their respiratory function during an infection of COVID-19 and may even put them at risk of pulmonary complications,⁶⁰ leading to a poor prognosis.⁶¹ Obesity is highly associated with obstructive sleep apnea (OSA),⁶² which can lead to repeated airway obstruction in patients with COVID-19, worsening pro-inflammatory processes in the lungs.⁶³ The negative effect of obesity on respiratory function may account for the higher risk of respiratory failure and necessity for mechanical ventilation in patients that have comorbid obesity with COVID-19.^{64–67}

4.2. Immune function and susceptibility

Previous studies have found that obesity is a risk factor for admission to the hospital for H1N1 influenza A⁴ and other respiratory infections.⁶⁸ This may be due to the fact that the baseline inflammatory state of obesity weakens the immune system's response to the virus, including systemic changes in the innate and adaptive responses, showing a delayed

and sluggish antiviral response to viral infection.⁶⁹ Patients with obesity have chronically high levels of leptin and low levels of adiponectin. This adverse hormonal state can also lead to a maladjusted immune response.⁷⁰ Obesity makes individuals more susceptible to viral infection, increasing the exposure of the virus and the long-term infection of hosts with obesity. Obesity also affected influenza virus clearance. Compared to adults of normal weight, the amount of RNA shedding and the duration of positive samples of the H1N1 virus were increased in adults with obesity.⁵ Obesity has also been shown to have a substantial impact on the immunity and pathogen defense, including the disruption of lymphoid tissue integrity and alterations in leukocyte development, phenotypes, and activity.⁷¹ In a prospective observational study of the trivalent inactivated influenza vaccine (IIV3) in adults, the results have shown that the initial serum conversion rates are higher in people with obesity, but the vaccine efficacy declines more over time than in people without obesity.⁷² This decline of vaccine efficacy may be due to the fact that overweight and obesity impairs vaccine response to pathogens. The immune-induced response of both obese adults and children is diminished,⁷³ and the vaccine-specific T cell responses of adults with obesity is weakened and impaired,⁷⁴ where T cells are necessary for the protection and recovery of viral infection.

4.3. Cytokine storm

Cytokine storm is an important cause of death among COVID-19 patients.⁷⁵ It represents a phenomenon of immune hyperactivation and is characterized by increased levels of IL-6, interferon (IFN)- γ , and other cytokines, causing consequences and symptoms related to immune activation. Although some studies have found that higher levels of proinflammatory cytokines in severe COVID-19 reflect an increased viral burden rather than an inappropriate host response that needs to be corrected,⁷⁶ inflammatory cytokines (IL-1 β , IL-1Ra, IL-6, IL-8, IL-18, and TNF- α) associated with cytokine storm are no different than those associated with severe ARDS or sepsis.⁷⁷ But the pro-inflammatory environment of individuals with obesity may further

exacerbate inflammation, exposing them to even higher levels of circulating inflammatory molecules.⁷⁸ Dysregulated immune and other inflammation-related responses of obesity patients may aggravate the cytokine storm and allow increased viral spread and extended infections, which accelerate the severity of COVID-19 in patients with obesity.

Individuals with obesity have a low level of systemic chronic inflammation, and the TNF- α , IL-6, or c-reactive protein (CRP) is higher, increasing the circulating level of pro-inflammatory cytokines.⁶¹ Clinical biochemical studies of COVID-19 metabolic obesity patients also found that IL-6 was significantly increased, and CRP was positively correlated with waist-to-hip ratio (WHR).⁷⁹ Excess fat is also associated with over-activation of the complement system, which is an important host mediator of virus-induced diseases and exacerbates inflammation.⁸⁰ Furthermore, the prevalence of vitamin D deficiency is higher among people with obesity. Vitamin D, which in detriment has been linked to various inflammations, infections, and lung diseases, can also increase the risk of systemic infections and damage the immune response. Together, they may make obesity a risk factor for “cytokine storms”.

There is no specific medicine to prevent SARS-CoV-2 infection and cytokine storm caused by the virus.⁸¹ Once the cytokine storm occurs, it is difficult for clinicians to reverse the adverse outcomes of patients. In addition to the exploration and research of drug therapy and new drugs, more attention should be given to warn patients of cytokine storms to achieve early detection and treatment, if necessary. It is of significance to suppress inflammatory response and support treatment. The changes of pulmonary imaging, respiratory function and laboratory indicators should be closely monitored, and once a patient's indicators fluctuate, they should be immediately transferred to the intensive care unit to suppress cytokine storm and prevent further intensification via medication and oxygen therapy.⁸²

4.4. Angiotensin-converting enzyme-2 (ACE-2)

The causes of variation in the inflammatory response in SARS-CoV-2 are unknown, but adipose tissue could contribute to this variation. Adipocytes, obesity-induced related inflammation, and immune system impairment may play an important role in infection by SARS-CoV-2.⁸³ Adipose tissue is among the tissues with the highest expression of the ACE2 receptor that binds the virus⁸⁴ and surrounds the heart and the connected vessels, opening the possibility that adipose tissue acts as a reservoir for the virus. In the COVID-19 infection, ACE2 is a binding receptor of the novel coronavirus. Since SARS-CoV-2 enters the host cells through ACE2 receptors after the spike protein is activated by host cell protease, the cells and tissues expressing ACE2 are potential targets of SARS-CoV-2. Tissue analysis showed that the ACE2 expression in adipose tissue is higher than that in lungs, suggesting that people with obesity are more susceptible to the novel coronavirus.⁸⁵ In addition, chronic activation of renin-angiotensin-aldosterone system (RAAS) in patients with obesity is conducive to the high expression of ACE-2 and the low availability of angiotensin 1–7, which reduces the antiviral immunity and increases the susceptibility to SARS-CoV-2.⁸⁶ However, no study has been conducted to elucidate the relationship between SARS-CoV-2 and adipose tissue, or the incidence of COVID-19 and obesity, which needs to be further verified by clinical studies.

4.5. Other potential mechanisms

Individuals with obesity are rich in epicardial adipose tissue (EAT), which can affect the cardiac function in patients with COVID-19 at an early stage. Moreover, EAT is a rich source of adipokines, including various pro-inflammatory mediators that contribute to inflammatory cytokine storms.⁸⁷ Obesity poses challenges to the patient's diagnosis and treatment, such as poor quality of diagnostic imaging, difficulties in airway management, and unresponsiveness to prone positioning.⁸⁸

5. Obesity prevention and management during COVID-19 pandemic

5.1. Prevention measures in patients with obesity

Targeted therapies with specific drugs and vaccines still need time to be developed, so we should focus on prevention for people with obesity. The general preventive measures for COVID-19 should follow the national or local prevention and control guidelines for hand hygiene, wearing protective equipment, reducing contact, and avoiding non-essential travel to major affected areas. Surveillance and control of co-existing chronic diseases need to be strengthened. For example, patients with diabetes and hypertension need to monitor their blood sugar and blood pressure more frequently.⁸⁹ The European Association for the Study of Obesity advises people with obesity to pay attention to energy intake (e.g., protein nutrients), energy expenditure (e.g., moderate physical activity and exercise in non-crowded areas during the period of quarantine), sleep (e.g., sleep duration and quality), and mental health and resilience (e.g., healthy mental conditions).⁹⁰ Patients with delayed bariatric outpatient follow-up appointments and bariatric surgery should adopt a healthier lifestyle during the epidemic; online weight management programs, evaluation of postoperative complications, and monitoring of weight loss response are also recommended.⁹¹

5.2. Measures in COVID-19 patients with obesity

Obesity increases the risk of severe COVID-19 progression, so we need to pay more attention to infection monitoring and clinical treatment in COVID-19 patients with obesity. Patients with obesity who have been exposed to COVID-19 patients or high-risk areas for COVID-19 infection, especially those who have subsequently developed suspected symptoms for COVID-19 (e.g., cold, coughing, runny nose, fever), should go to a medical institution for virus testing as soon as possible⁹²; those having mild symptoms can be consulted at home through telemedicine and should be self-isolated for 14 days after their symptoms disappear. COVID-19 patients with obesity aged over 60 should be referred to a hospital as soon as possible. Patients with other basic or chronic diseases (e.g., diabetes, hypertension, heart diseases) should seek medical attention urgently. During the treatment, they should continue to strictly comply with appropriate control of blood glucose, blood pressure, and blood lipids; appropriate hypoglycemic, hypotensive, and lipid-lowering regimens should be continued during the treatment.⁹³ Inflammatory response indicators (IL-6, TNF- α , CRP) and immune response indicators (immunoglobulin, CD4+, CD8+) should be monitored during treatment to prevent “cytokine storms” in a timely manner. When treating individuals with obesity, the feasibility of operations and appropriate tools should be considered in advance to avoid delay in treatment.

5.3. Impact of COVID-19 lockdown on body weight

We also suggest that everyone should control their weight gain during the epidemic period of COVID-19, so as to avoid the development of obesity, thus increasing the risk of infection and progression to severe stage of COVID-19. At present, many countries and regions around the world adopted lockdown and school suspension measures to reduce the spread of the virus and recommended social isolation to reduce the risk of infection. Knowing that summer vacation may be a risk factor for students' weight gain,⁹⁴ we suspect that isolation during the outbreak may enhance the risk factors for obesity and weight gain. Studies have estimated that the prevalence of COVID-19 may double the number of out-of-school hours for children in the US⁹⁵, and that prolonged isolation at home may lead to changes in personal lifestyles, sleep patterns, commuting style and psychological state, thereby indirectly affecting weight change. Some recent studies showed that young people tended to display unfavorable lifestyle changes during and after lockdown, including unsafe, hyper-processed, high-calorie diets, and

decreased exercise time, increased screen time, and an increased amount of sleep.⁹⁶⁻⁹⁹ Furthermore, active commuting, including public transportation, walking, and cycling, was significantly associated with decreased BMI and body fat percentages among men and women.¹⁰⁰ A study in China found that isolation and the rapid spread of SARS-CoV-2 led participants to exhibit higher levels of anxiety, depression, and lower levels of mental health,¹⁰¹ and other mediating factors, such as diet and amount of sleep, that influence weight change.¹⁰² Rumors and information overload increase stress, which can also affect weight through biological behavioral and psychological mechanisms.¹⁰³

6. Future directions and conclusions

The COVID-19 pandemic is characterized by a high incidence of severe and acute organ damage, especially the lungs with SARS, but also acute cardiovascular events, in association with a pro-inflammatory cytokine-related storm.¹⁰⁴ Such severe acute events are particularly prevalent among aged individuals and patients with co-morbidities such as obesity, hypertension, and Type 2 diabetes which have emerged as major contributors to the severity of symptoms and organ failure, whilst the current studies report a lower prevalence of severe COVID-19 infection among smokers and people with chronic lung diseases. These observations suggest the importance of the “metabolic disease exposome”,¹⁰⁵ including dietary lifestyle, glycaemic disorders, obesity, and sedentariness, among other potential disease severity modifiers, such as systemic hypertension and aging, leading to chronic low-grade inflammation, which may aggravate COVID-19-induced acute organ failure.

Therefore, it is essential to precisely identify the factors underlying the severity and the clinical presentation of the disease, especially when considering the risk of additional waves of COVID-19.¹⁰⁶ Obesity is a risk factor for severe forms of COVID-19, through physiological, biochemical, immune, and anatomical mechanisms. Indeed, many countries worldwide are currently under lockdown to curb the dramatic increase in the number of patients in critical conditions. Staying at home during the COVID-19 pandemic also mediates changes in lifestyles and sleep patterns that increase the risk of obesity.¹⁰⁸⁻¹¹⁰ Thus, the identification of optimal strategies to manage the health crisis after the lockdown is of critical importance for the decision makers on the management of the COVID-19 health crisis. One of those strategies would be the identification of vulnerable subjects in order to adapt social distancing strategies, using a personalized approach targeting this population at risk.

Based on the characteristics of people with obesity, we suggest that individuals with obesity should not only follow the general preventive measures and health guidance but should also pay more attention to the control of other underlying diseases. Patients should seek the help of medical staff as soon as possible after being infected with the virus. The treatment of basic diseases should be considered in the treatment process, and the condition indicators should be closely monitored to alleviate the prognosis. In addition, we also recommend the use of telemedicine for obesity training and education.

Some limitations in this review should also be mentioned, so future efforts could be built upon it. We covered several related themes and used a variety of indicators (e.g., recovery time, ICU admission, IMV necessity, death) to systematically examine the additional burden of obesity on patients with COVID-19, the impact of COVID-19 infection on which are difficult to be compared and quantified. Therefore, we could not conduct a series of meta-analyses of high quality to accompany this systematic review. Also, to include more national and regional studies to make this review more informative and convincing, we did not adopt a uniform criterion for obesity (e.g., BMI cutoff values) to filter the literature. Stratifying the included studies by different criteria of obesity is also expected to be realized in future as the number of studies is increasing.

Determining the association between obesity and COVID-19 will require large, national or international, retrospective medical studies and autopsy studies. In the follow-up clinical treatment, it is important to measure and collect the parameters of human obesity, including height, weight, waist circumference, hip circumference, etc. Priority should be given to the treatment of COVID-19 patients with obesity to properly allocate medical resources.

CRedit authorship contribution statement

All author read and approved the final version of the manuscript.

Declaration of competing interest

All authors declare no competing interests.

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