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COVID-19

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Effect of obesity and body mass index on coronavirus disease 2019 severity: A systematic review and meta-analysis

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Summary

We conducted a systematic review of observational studies to examine the effects of body mass index (BMI) and obesity (BMI ≥ 30 kg/m^2) on coronavirus disease 2019 (COVID-19). Medline, Embase, and the Cochrane Library were searched. Sixteen articles were finally included in the meta-analysis, and a random effects model was used. BMI was found to be higher in patients with severe disease than in those with mild or moderate disease (MD 1.6, 95% CI, 0.8–2.4; p = .0002) in China; however, the heterogeneity was high (I^2 = 75%). Elevated BMI was associated with invasive mechanical ventilation (IMV) use (MD 4.1, 95% CI, 2.1–6.1; p < .0001) in Western countries, and this result was consistent across studies (I^2 = 0%). Additionally, there were increased odds ratios of IMV use (OR 2.0, 95% CI, 1.4–2.9; p < .0001) and hospitalization (OR 1.4, 95% CI, 1.3–1.60; p < .00001) in patients with obesity. There was no substantial heterogeneity (I^2 = 0%). In conclusion, obesity or high BMI increased the risk of hospitalization, severe disease and invasive mechanical ventilation in COVID-19. Physicians must be alert to these early indicators to identify critical patients.

KEYWORDS
BMI, COVID-19, obesity, severe disease

1 | INTRODUCTION

Coronavirus disease 2019 (COVID-19) is an emerging viral disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). A quick response from governments or societies to the crisis may protect the interests of their citizens.[1] Understanding the disease and its risk factors is the key point in implementing public health policy.

The spectrum of COVID-19 varies from asymptomatic, upper respiratory symptoms and pneumonia to acute respiratory distress syndrome (ARDS). Several risk factors have been proposed to be associated with severe disease or death in COVID-19. In clinical studies among countries, old age is the most important factor and may be related to a decreased immune response to viral infection.[2,3] Patients with underlying diseases were more likely to receive intensive care or develop ARDS. Hypertension, cardiovascular disease and diabetes are common comorbidities mentioned in the current literature.[4–6]

People with obesity are prone to develop severe diseases after infections. For example, nearly one-third of hospitalized patients and fatal cases were found to be comorbid with obesity during the 2009 H1N1 influenza A virus pandemic.[7,8] Preexisting high levels of circulating leptin-induced cytokine dysregulation in obese animals have been proposed to be a cofactor for influenza-related mortality.[9] Because the prevalence of obesity is increasing globally, the impact of obesity on infectious diseases, especially the newly emerging infectious disease COVID-19, may need further exploration.

Obesity may affect the status of immune function and provoke chronic inflammation as well as increase the cardiovascular load and risk of metabolic disorders.[10] As a consequence, we hypothesize that obesity may increase the risk of severe COVID-19 through the above mechanisms. Because comprehensive reviews of obesity and COVID-19 are limited, we initiated this study to clarify the role of obesity in this emerging disease. The aims of this study were to evaluate the risk of severe COVID-19 in patients with obesity and to investigate whether BMI was different between severe and non-severe cases.

2 | METHOD

2.1 | Search strategy

The study was conducted following the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement. We performed a systematic literature search in three major electronic databases: Medline, Embase and Cochrane Library. We combined the following terms: "coronavirus or COVID-19 or 2019-nCoV or SARS-CoV-2," "clinical features or characteristics or symptoms," "survival or mortality," "severe disease or intensive care" and "mechanical ventilation" to find related reports. The time period was restricted to literature published beginning in January 2020, since SARS-CoV-2 was identified then. We have provided a detailed search strategy in Table A1. Available full texts and the reference lists of the relevant studies were retrieved; there was no language restriction in our search. Google Scholar was searched manually for possible missing articles. The last update of the study was on 30 May 2020.

Three independent reviewers (THC, CCC and LYC) screened all titles and abstracts for eligibility. Studies were eligible for inclusion if they met the following criteria: (1) COVID-19 was confirmed by detection of SARS-CoV-2 via polymerase chain reaction (PCR); (2) studies included patient characteristics and clinical features; and (3) the obesity prevalence or body mass index (BMI) data of the patients was reported. Correspondences or letters fulfilling the above criteria were also included. We carefully screened the enrolling hospitals and study periods to avoid repeated calculation and double counting of patients. Studies were excluded for the following reasons: (1) clinical diagnosis of COVID-19 without PCR confirmation; (2) participants included children and pregnant women, whose physiological status and body fat distribution are unique compared with the general population; and (3) case series with fewer than 10 patients, because some outliers may easily affect the mean or median.

2.2 | Data extraction

After full-text screening for eligibility and review, two reviewers (THC and LYC) extracted data independently. Disagreements were resolved by consensus or review by another reviewer. The following variables were extracted from each study if available: author information, journal, year of publication, study country, study period, demographic data, BMI, obesity prevalence, disease severity and invasive mechanical ventilation (IMV) use.

2.3 | Quality and risk of bias assessment

The quality of nonrandomized studies included in the meta-analysis was assessed using the Newcastle–Ottawa Scale (NOS). The maximum score for each study was 9, and articles with poor quality (score = 0–3) were excluded. After qualitative and quantitative synthesis, we used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach to evaluate the confidence in the estimate of effect of the included studies. The factors considered in determining the quality of the evidence were risk of bias, imprecision, indirectness, inconsistency of results, publication bias, dose-effect response, magnitude of the effect and plausible confounders. Evidence was finally graded as high, moderate, low or very low quality. The evidence summary for this meta-analysis was prepared in GRADEpro Guideline Development Tool Software (McMaster University, 2015, developed by Evidence Prime, Inc.).

2.4 | Outcomes and data analysis

Separate analyses were conducted according to different outcomes: (1) hospitalization or discharge from the emergency department; (2) severe or nonsevere disease; and (3) IMV use during hospitalization. The disease severity was classified based on two guidelines published by the American Thoracic Society (ATS)/Infectious Diseases Society of America (IDSA)[11] and the National Health Commission of China.[12] The World Health Organization (WHO) defines obesity as BMI ≥ 30, while BMI ≥ 28 is the optimal cutoff value for Chinese adults.[13] In studies conducted in Western countries, both BMI and obesity prevalence were used to assess outcomes if available. However, some studies in China still defined obesity as BMI ≥ 25. Thus, to avoid confusion, we used BMI instead of obesity prevalence to assess outcomes in Chinese studies. In our meta-analysis, we calculated the odds ratio (OR) for the dichotomous outcome (obesity prevalence) and mean difference (MD) for the continuous data (BMI) with their 95% confidence intervals (CIs) by random effects models in this meta-analysis. If studies reported only median values with interquartile ranges alone, we derived means and standard deviations using statistical methods described by Chen et al.[14] and Gao et al.[15] We used Review Manager (RevMan) (Computer programme), version 5.3 (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014.) for the analysis and conducted a meta-analysis when at least two studies with available data reported the same outcome. I^2 was calculated to measure statistical heterogeneity across the included studies. $I^2 > 50\%$ and $p < .05$ were considered substantial heterogeneity. Publication bias was not assessed for outcomes fewer than 10 studies.

3 | RESULT

3.1 | Study selection

Figure 1 shows the flow diagram of the study selection process. A total of 7140 articles were identified in the initial search. After removing 3446 duplicates, 3694 were screened by titles and abstracts, and obviously irrelevant articles were excluded. The remaining 75 were

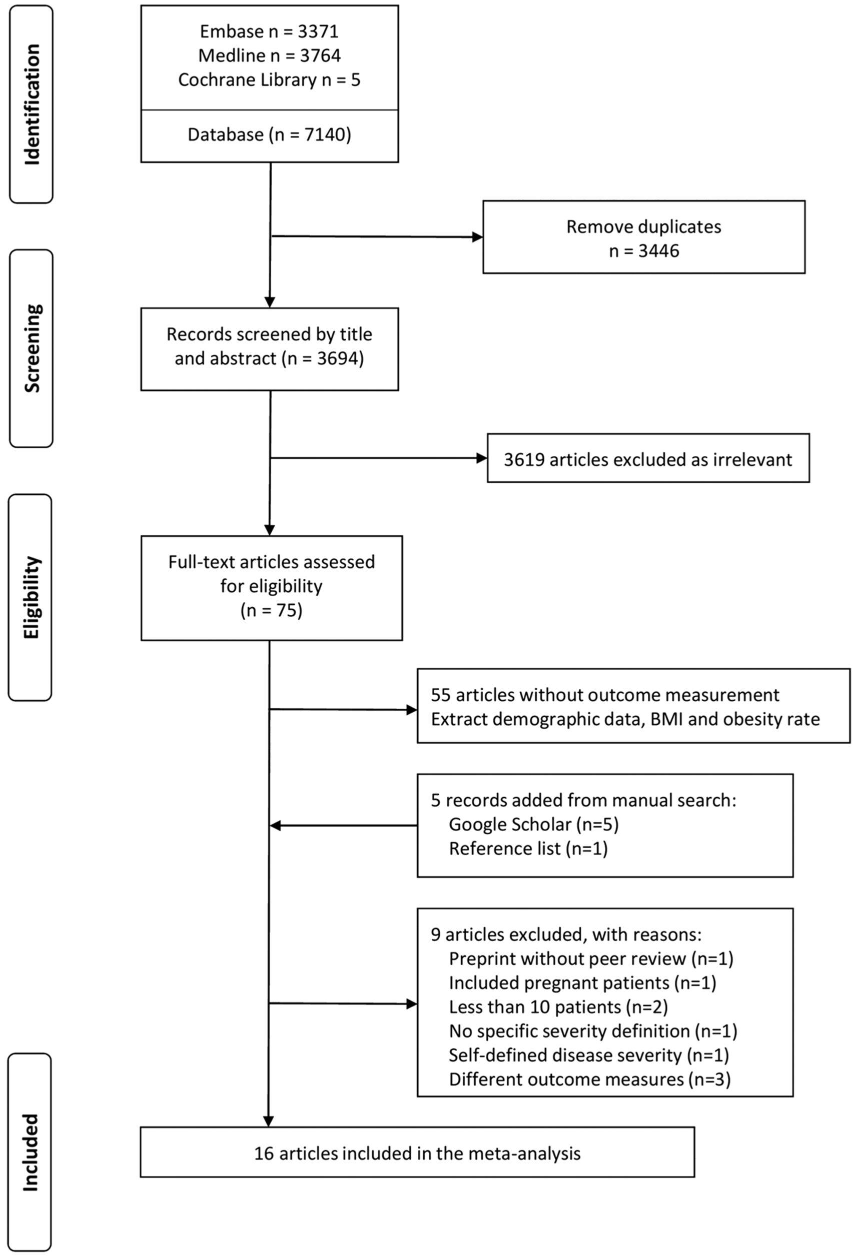

FIGURE 1 Flow diagram of the study selection process

retrieved for full-text assessment. Of these, only BMI or obesity prevalence were reported in 55 articles. We extracted demographic data independently. Nineteen articles were selected for qualitative synthesis, and five records were identified through manual searches of Google Scholar (n = 5) and the reference list (n = 1). Finally, we excluded nine articles: One report was a preprint manuscript without peer review; three case series included pregnant women or case numbers <10; two reports used self-defined severity or did not include a specific definition; and three reports demonstrated different outcome measures compared with other studies, so the data could not be pooled together for quantitative synthesis. These three reports demonstrated the outcome as the presence of pneumonia, ARDS and disease progression, which were different from those of other studies. Therefore, articles with these different outcome measures were not included in our meta-analysis. Finally, we extracted data from 16 articles for meta-analysis.

3.2 | Study characteristics

In Table A2, we summarize the characteristics of the current literature with the BMI and obesity data of COVID-19 patients. BMI and obesity (defined as BMI ≥ 30) data from each study are depicted in Figure 2. The global age-standardized mean BMI (24.2 kg/m^2) of men[16] and the mean prevalence of obesity in adults (19.5%) provided by the Organisation for Economic Cooperation and Development (OECD)[17] were drawn on top of the figure for comparison.

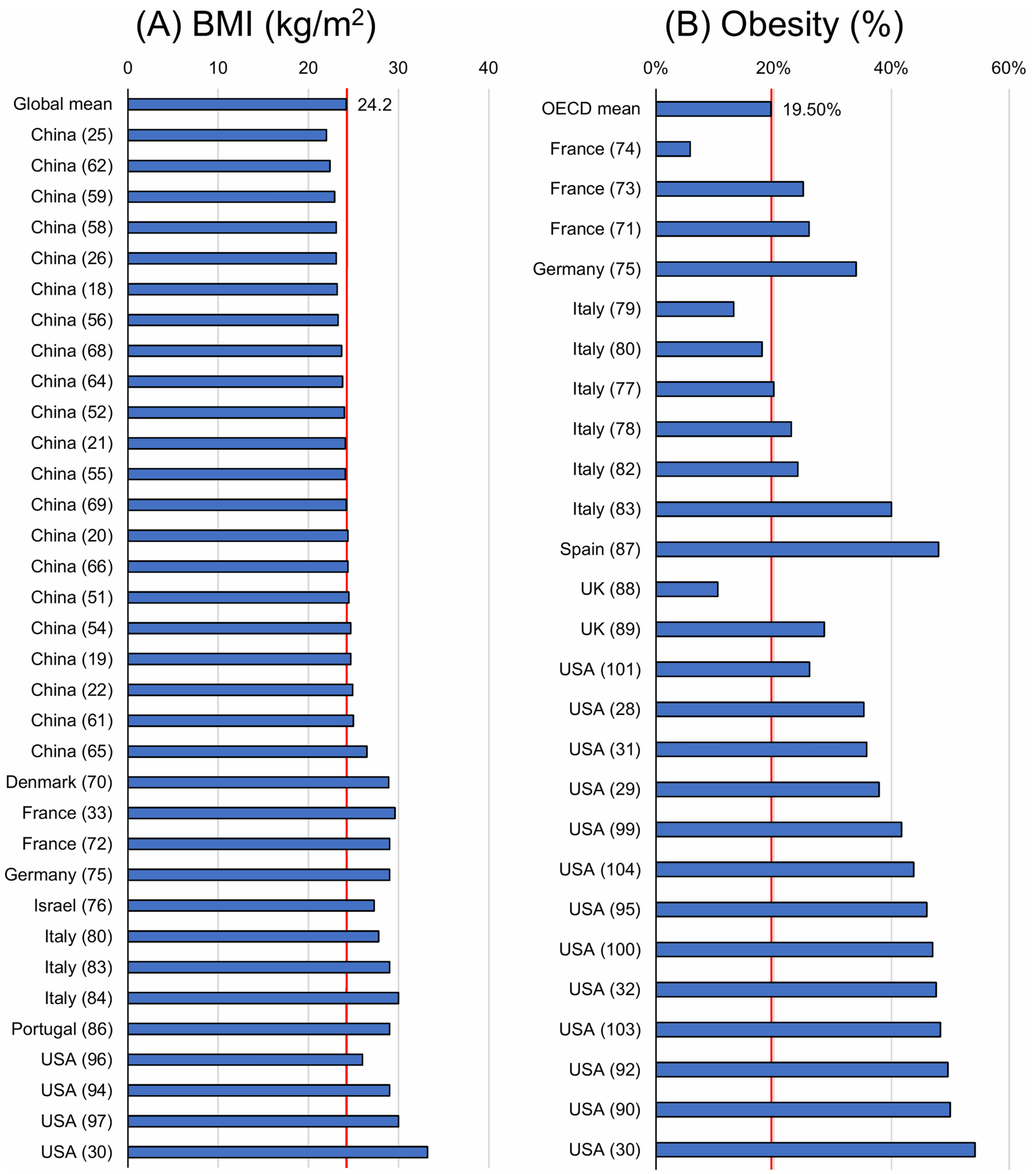

FIGURE 2 (A) BMI (kg/m^2) data from current studies compared with global age-standardized mean BMI (24.2 kg/m^2) of men. (B) Obesity (%) (defined as BMI ≥ 30) in the current literature compared with the Organisation for Economic Cooperation and Development (OECD) mean prevalence of obesity in adults (19.5%). The reference and detailed characteristics of each included study are provided in Table A2

After full-text review, 16 articles were selected for quantitative synthesis (Table 1).[18-33] The median or mean age ranged from 35 to 67 years old with a mortality rate from 0% to 50%. Male predominance was found in 10 studies. Ten studies were conducted in China from January 1 to March 11. Five studies were reported from different hospitals in Wuhan, the epidemic area in China. The enrolled populations were different in three studies. Liu et al. focused on hospitalized health workers,[24] Peng et al. put emphasis on patients with cardiovascular comorbidity,[25] and Xiong et al. collected data from patients undergoing haemodialysis.[26] The outcome measure in these articles was disease severity, which was categorized into severe or nonsevere groups. However, different severity definitions were applied. We further categorized outcomes into two subgroups, which included guidelines published by the ATS and IDSA[11] and the National Health Commission of China.[12]

Another six reports retrospectively collected data from countries outside China: five in the United States and one in France. The outcomes measured in these studies were as follows: (1) the association between obesity and hospitalization for patients being treated in the emergency department; (2) the association between obesity and patients receiving IMV; and (3) the association between BMI and IMV use.

TABLE 1 Characteristics of the included studies assessing severe COVID-19 according to BMI and obesity

Study	Country	Language	Sample (male)	Age (year)	Severe group (BMI or obesity prevalence)	Nonsevere group (BMI or obesity prevalence)	Death (%)
Outcome measurement: severe or nonsevere disease by American Thoracic Society and Infectious Diseases Society of America classification[11]							
Cai[18]	China	English	298 (49%)	48	24.5 (22–27.8)	22.9 (20.6–25.2)	1
Li[19]	China	English	548 (51%)	60	25.3 (22.4–27.6)	24.5 (22.4–26.0)	16.5
Outcome measurement: severe or nonsevere disease by National Health Commission of China classification[12]							
Huang[20]	China	English	202 (57%)	44	26.4 (23.7–29.5)	24.2 (22.1–26.1)	0
Wu[21]	China	English	280 (54%)	43	25.8 ± 1.8	23.6 ± 3.2	0
Xiang[22]	China	Chinese	49 (67%)	43	26.2 ± 3.93	24.6 ± 4.0	-
Chen[23]	China	English	145 (55%)	48	24.8 (23.1–27.0)	23.2 (21.7–25.7)	-
Liu[24]	China	Chinese	30 (33%)	35	22.0 ± 1.3	27.0 ± 2.5	0
Peng[25]	China	Chinese	112 (47%)	62	25.5 (23.0–27.5)	22.0 (20.0–24.0)	15.2
Xiong[26]	China	English	131 (57%)	63	22.6 ± 3.7	23.3 ± 4.1	-
Sun[27]	China	English	57 (51%)	-	24.0 (21.5–26.0)	26.8 (23.0–29.9)	-
Outcome measurement: hospitalization or discharge from emergency department (definition of obesity: BMI ≥ 30)							
Petrilli[28]	USA	English	5,279 (49.5%)	54	39.5%	30.8%	-
Lighter[29]	USA	English	3,615	-	42.5%	33.5%	-
Outcome measurement: invasive mechanical ventilator (IMV) use (obesity: BMI ≥ 30)							
Bhatraju[30]	USA	English	24 (63%)	64	61%	40%	50
Goyal[31]	USA	English	393 (61.2%)	60	43.4%	31.9%	10.2
Kalligeros[32]	USA	English	103 (61%)	62	65.5%	40.5%	-
Simonnet[33]	France	English	124 (73%)	60	53.9%	31.4%	15

Note: Data are shown as mean ± SD or median (IQR) or number (%). Age (year) is expressed as median or mean age in year.
Abbreviations: BMI, body mass index; COVID-19, coronavirus disease 2019; IMV, invasive mechanical ventilation; IQR, interquartile range; SD, standard deviation.

3.3 | Associations between obesity and hospitalization

In Figure 3, two studies in New York show that obesity was related to hospitalization during emergency department visits (OR 1.4, 95% CI, 1.3–1.6; $p < .00001$). There was no substantial heterogeneity ($I^2 = 0\%$, $p = .53$).

3.4 | Associations between elevated BMI and severe disease

Figure 4A shows 10 studies in China exploring the relation between BMI and disease severity. We performed subgroup analysis according to two classification guidelines. In studies adhering to the ATS/IDSA guidelines, BMI was higher in patients with severe disease than in

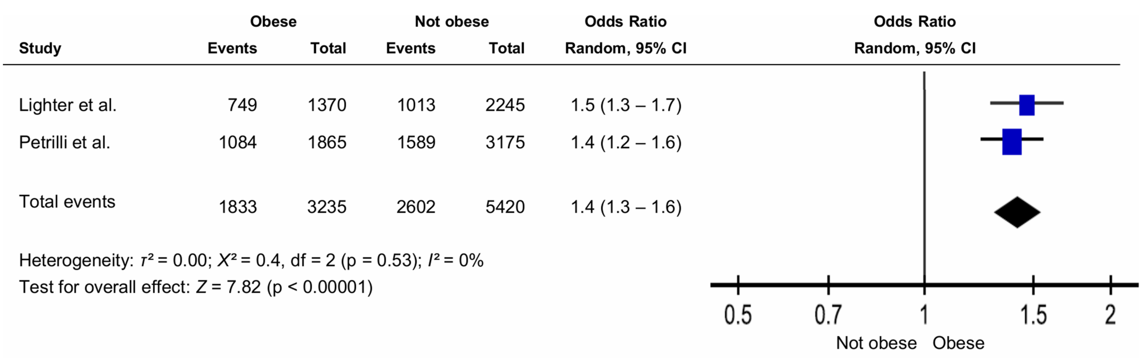

FIGURE 3 Associations between obesity and hospitalization in patients with COVID-19

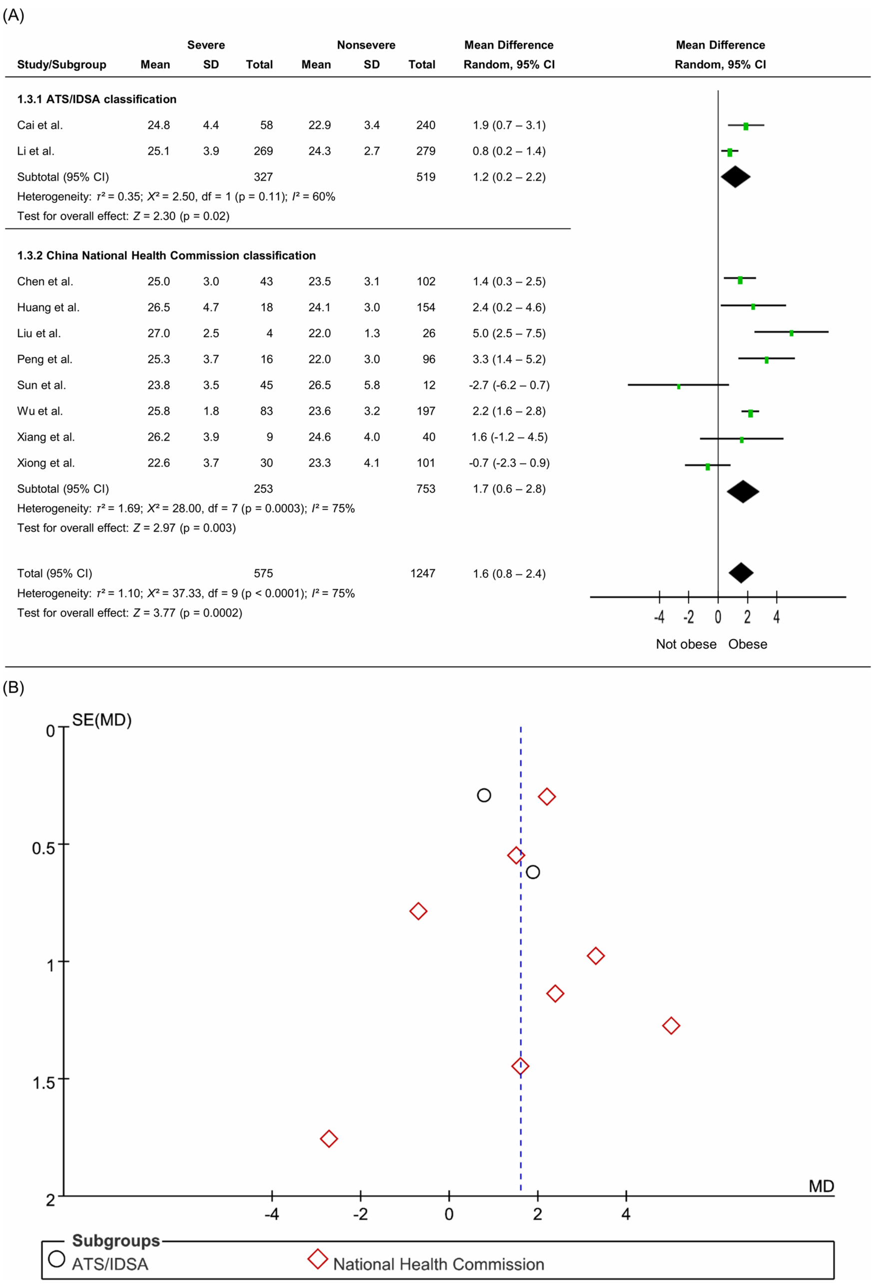

FIGURE 4 (A) Associations between elevated BMI and severe COVID-19, grouped by different severity classifications. (B) Funnel plots of studies reporting the associations between BMI and severe COVID-19

those with mild or moderate disease in two studies (MD 1.2, 95% CI, 0.2–2.2; p = .02). For studies using the National Health Commission of China classification, BMI was also higher in patients with severe disease than in mild to moderate patients (MD 1.7, 95% CI, 0.6–2.8; p = .003). However, high overall heterogeneities within each group were observed (I^2 = 60%, p = .11; I^2 = 75%, p = .0003). There was no evidence of publication bias (Figure 4B).

3.5 | Associations between elevated BMI and IMV use

Two studies demonstrated the effect of elevated BMI on IMV use. Figure 5 shows that elevated BMI was associated with IMV use (MD 4.1, 95% CI, 2.1–6.1; p < .0001), and the result was consistent without heterogeneity (I^2 = 0%; p = .66).

3.6 | Associations between obesity and IMV use

Figure 6 includes four studies from areas outside China. In these studies, obesity was defined as BMI ≥ 30 kg/m^2. There was an increased OR of IMV use in patients with obesity (OR 2.0, 95% CI, 1.4–2.9; p < .0001), and no significant heterogeneity was found in the studies included (I^2 = 0%; p = .43).

3.7 | Quality of evidence

Table 2 shows a summary of the GRADE evidence profile for our meta-analysis. In a meta-analysis of observational studies, the initial rating starts as low quality of evidence. For increased risk for hospitalization during emergency department visits, the certainty was “low.”

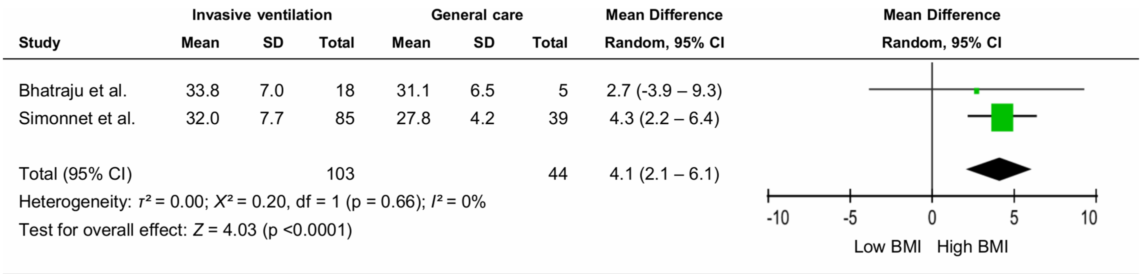

FIGURE 5 Associations between elevated BMI and invasive mechanical ventilation (IMV) use in patients with COVID-19

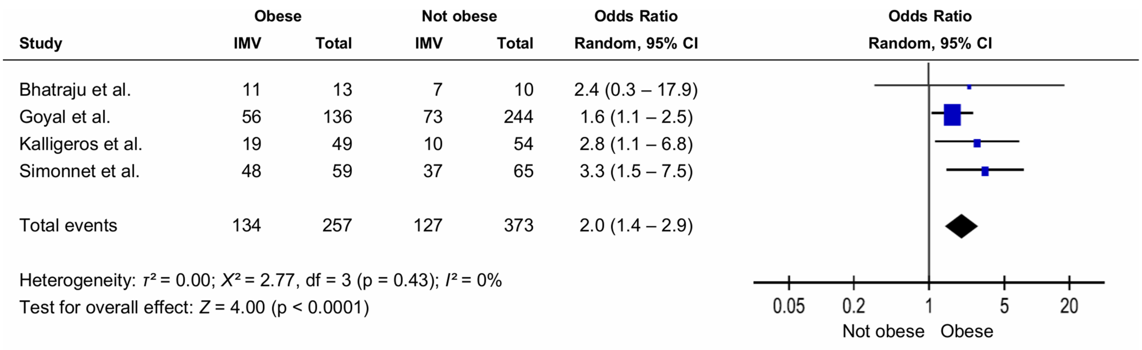

FIGURE 6 Forest plots comparing the pooled odds ratio of invasive mechanical ventilation (IMV) use between patients with or without obesity

TABLE 2 Summary of GRADE evidence profile and certainty of evidence on the effects of high BMI or obesity on COVID-19 severity

Certainty assessment						
Patients (studies)	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence
Obesity and hospitalization during emergency department visit						
8655 patients (2 observational studies)	Not serious	Not serious	Not serious	Not serious	None	⊕⊕ Low
Elevate BMI and severe disease						
1822 patients (10 observational studies)	Not serious	Serious[a]	Not serious	Not serious	None	⊕ Very low
Elevate BMI and invasive mechanical ventilator use						
147 patients (2 observational studies)	Not serious	Not serious	Not serious	Not serious	None	⊕⊕ Low
Obesity and invasive mechanical ventilator use						
630 patients (4 observational studies)	Not serious	Not serious	Not serious	Not serious	None	⊕⊕ Low

Note: Explanations
a. Include different populations (ex: health care worker or patients with underlying cardiovascular disease) that caused increased heterogeneity.
Abbreviations: BMI, body mass index; COVID-19, coronavirus disease 2019; GRADE, Grading of Recommendations Assessment, Development and Evaluation.

For the association between elevated BMI and severe disease, the certainty was "very low" because of downgrades for inconsistency. For the risk of IMV use in patients with obesity and elevated BMI, the overall certainty was "low."

4 | DISCUSSION

In this review, we summarized the increased risks of high BMI or obesity on severe COVID-19 based on current published data. The BMI data and obesity prevalence in this review varied, which can primarily be explained by regional and ethic differences. Under the definition of BMI ≥ 30 kg/m^2, obesity may be prevalent in >30% of the population in some countries, such as the United States, Mexico or New Zealand. However, in China, Japan, Korea or some other Asia-Pacific countries, the prevalence of obesity was <10%.[34,35] The low prevalence of obesity led to studies in Asia seldom considering high BMI or obesity to be a risk factor for severe disease. From the epidemiological data on the obesity prevalence in our review, the Asian definition of obesity is another consideration. Both definitions of BMI ≥ 30 and BMI ≥ 28 as obesity were used in some studies conducted in China. To avoid confusion, we used BMI instead of obesity prevalence to explore the risk of severe disease. Additionally, we did not pool the data from China with those from Western countries.

Studies in China showed a statistically significant MD in BMI between severe and nonsevere disease. Small case numbers and various study populations may explain the heterogeneity despite subgroup analysis according to severity definition. In studies with younger age groups, such as medical workers[24] or asymptomatic patients[36] such participants had low BMI and low prevalence of comorbidities compared with the general hospitalized population. In one report exploring patients with underlying metabolic-associated fatty liver disease,[37] the subjects presented with the highest mean BMI across the included articles from China. In populations with a high prevalence of comorbidities, such as hypertension or cardiovascular disease, the effect of these risk factors may also need to be considered. Because background population obesity prevalence might influence outcomes,[38] the results are more consistent in Western countries. Patients with obesity or higher BMI showed significantly increased odds of receiving intensive mechanical ventilation or even hospitalization. Similar data have been reported by Kass et al. indicating that obesity could be an independent risk factor for severe COVID-19.[39]

Obesity is also an independent risk factor for some infections. After surgery, obesity is associated with a 1.1-fold to 4.4-fold increase in the adjusted odds of developing surgical site infection compared with normal weight.[40] In a population-based study, obesity was independently associated with future sepsis.[41] Moreover, obesity is a risk factor for community-acquired pneumonia and influenza-related pneumonia.[42] In institutionalized geriatric patients, obesity is associated with an overall increased infection rate.[43] In summary, healthy weight is an essential part of health promotion and disease prevention, even in infectious diseases.

The possible mechanism and pathophysiology of obesity and severe COVID-19 could be explained in several aspects. First, infection with SARS-CoV-2 reduces angiotensin-converting enzyme-2 (ACE 2) activity and causes dysregulation of the renin-angiotensin system.[44] As a result of increased angiotensin II, lung injury or tissue damage may occur. ACE 2 receptors are highly expressed in adipose tissue, and patients with obesity tend to have larger quantities of adipose tissue than the general population, partially explaining the severity. Second, impaired T or B cell immunity was found in patients with obesity. In some animal models, the cytotoxic response and influenza-specific CD8 + memory T cells of obese mice decreased significantly.[45,46] In SARS-CoV-2 infections, lymphopenia and an increased neutrophil-to-lymphocyte ratio usually indicate severe disease and poor outcome.[47,48] Obesity might be associated with relatively low immunity during the early phase of SARS-CoV-2 infection. Third, obesity is an important predisposing factor for some comorbidities in severe COVID-19. For example, increasing fat mass and unhealthy weight gain, even in childhood, may lead to increased carotid intima media thickness and further development of cardiovascular disease.[49] Last, ARDS is the major complication and cause of death in COVID-19. From the view of respiration, obesity plays a crucial role in ventilation, and patients with obesity show changes in baseline physiology. Ventilation and gas exchange are also impaired. Thus, the wide distribution of adipose tissue and systemic involvement is a possible explanation for the association between severe COVID-19 and obesity. Adipose tissue can be a research model to help understand the pathogenesis of COVID-19 infection and develop an effective treatment.[50]

There are several limitations in our study. First, the quality of evidence is low due to limited studies and small case numbers. Most of the enrolled articles were observational or retrospective studies, BMI data were scarce in the currently available literature, and we lacked BMI databases. Therefore, we need more high-quality and long-term follow-up studies to support the evidence. Second, we cannot address the issue between SARS-CoV-2 infection and increased body weight. The spectrum of COVID-19 has not been fully understood with underestimated asymptomatic or mild cases, so we failed to identify other control groups (healthy controls or asymptomatic patients) in this review. Third, obesity is a complex disorder with multisystem involvement. The relationship and interaction between other risk factors, such as age, diabetes, hypertension and cardiovascular disease, cannot be adjusted in this study. Meta-regression is a feasible method for dealing with this issue if more studies become available. Fourth, the demographic results are diverse in the included studies. Large-scale or population-based studies are needed.

To conclude, obesity or high BMI increased the risk of hospitalization, severe disease and IMV in COVID-19. Physicians must be alert to these early indicators to identify critical patients.

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APPENDIX A.

TABLE A1 Database search strategies

Search terms genetic trait	
English synonyms	**Controlled vocabulary Emtree/MeSH**
Coronavirus	Coronavirinae
COVID-19	Coronaviridae
2019-nCoV	Coronaviridae infection
SARS-CoV-2	Covid 19
	Sars coronavirus 2
	CORONAVIRUS
	CORONAVIRUS INFECTIONS
Clinical features	Clinical feature
Characteristics	
Symptoms	Symptom
	SYMPTOM ASSESSMENT
Survival	Survival
	SURVIVAL
Mortality	Mortality
	MORTALITY
Severe disease	Disease severity
Intensive care	Intensive care
	CRITICAL CARE
Mechanical ventilation	Artificial ventilation
	RESPIRATION, ARTIFICIAL

Search strategy			
Database	**#**	**Search syntax**	**Citations found**
Embase	1	(coronavirus OR "COVID-19" OR "2019-nCoV" OR "SARS-CoV-2"): ti,ab,kw,de	30 026
	2	"Coronavirinae"/exp OR "Coronavirinae"/exp OR "Coronaviridae infection"/exp OR "covid 19"/exp OR "sars coronavirus 2"/exp	28 193
	3	(clinical features OR characteristics OR symptoms OR survival OR mortality OR severe disease OR intensive care OR mechanical ventilation):ti,ab,kw,de	114 321
	4	"clinical feature"/exp OR "symptom"/exp OR "Survival"/exp OR "Mortality"/exp OR "disease severity"/exp OR "intensive care"/exp OR "artificial ventilation"/exp	4 395 276
	5	(#1 OR #2) AND (#3 OR #4)	7413
	6	#5 AND [2020]/py	3371
MEDLINE	1	(coronavirus OR "COVID-19" OR "2019-nCoV" OR "SARS-CoV-2").mp	30 701
	2	exp "CORONAVIRUS"/OR exp "CORONAVIRUS INFECTIONS"/	19 014
	3	(clinical features OR characteristics OR symptoms OR survival OR mortality OR severe disease OR intensive care OR mechanical ventilation).mp	3 988 238
	4	exp "SYMPTOM ASSESSMENT"/ OR exp "SURVIVAL"/ OR exp "MORTALITY"/ OR exp "CRITICAL CARE"/OR exp "RESPIRATION, ARTIFICIAL "/	507 048
	5	(1 OR 2) AND (3 OR 4)	7016
	6	limit 5 to (yr = "2020")	3764

TABLE A1 (Continued)

Search strategy			
Database	**#**	**Search syntax**	**Citations found**
CochraneCENTRAL	1	(coronavirus OR "COVID-19" OR "2019-nCoV" OR "SARS-CoV-2"): ti,ab,kw	359
	2	[mh "CORONAVIRUS"] OR [mh "CORONAVIRUS INFECTIONS"]	186
	3	(clinical features OR characteristics OR symptoms OR survival OR mortality OR severe disease OR intensive care OR mechanical ventilation):ti,ab,kw	386 174
	4	[mh "SYMPTOM ASSESSMENT"] OR [mh "SURVIVAL"] OR [mh "MORTALITY"] OR [mh "CRITICAL CARE"] OR [mh "RESPIRATION, ARTIFICIAL "]	14 963
	5	(#1 OR #2) AND (#3 OR #4)	248
	6	limit #5 to (yr = "2020")	17
	7	Cochrane reviews	5
	8	Special collections	1
	9	Trials	11

TABLE A2 Characteristics of current literature related with COVID-19 and BMI/obesity

Reference (first author)	Region	Country	Population	Case numbers	Mean/median age	Male ratio (%)	Common comorbidities (HTN, CVD, DM) (%)	Descriptions of BMI (median, IQR; mean ± SD) or obesity (%)
Wei[51]	Anhui	China	Hospitalized patients	167	42.3	56.9	CVD: 14.4, DM: 6.6	BMI: 24.5 ± 3.4
Ji[52]	Anhui and Beijing	China	Hospitalized patients	202	44.5	55.9	-	BMI: 24.0 ± 2.8
Wu[21]	Anhui and Jiangsu	China	Hospitalized patients	280	43.1	53.9	CVD: 20.4	BMI: 24.1 ± 3
Yu[53]	Dongguan	China	Hospitalized patients	95	-	55.8	-	BMI (with ARDS): 24.26 ± 3.32 BMI (without ARDS): 22.64 ± 3.55
Zhu[54]	Hefei	China	Patients visit emergency departments	32	46	47	HTN: 22, CVD:6, DM:13	BMI: 24.7 ± 3.2
Zhou[55]	Hubei	China	Severe or critical patients	21	66.1	61.9	HTN: 47.6, CVD: 38.1, DM: 23.8	BMI: 24.1 ± 2.0
Li[56]	Hubei and Shanghai	China	Patients with COVID-19 pneumonia	154	59	49.4	-	BM: 23.3 ± 1.9
Huang[20]	Jiangsu	China	Hospitalized patients	202	44	57.4	HTN: 14.4, CVD: 2.5, DM: 9.4	BMI: 24.4 (22.3–26.4) BMI ≥ 28: 14%
Xiang[22]	Nanchang	China	Hospitalized patients	49	42.9	67.3	HTN: 12.2, DM: 4.1	BMI: 24.9 (17.9–41.1)
Yu[57]	Shanghai	China	Hospitalized patients	26	65	76.9	HTN: 34.6, DM: 19.2	BMI ≥ 24: 60%
Cai[58]	Shenzhen	China	Hospitalized patients	417	47	47.5	HTN: 13.9, DM: 5.5	BMI: 23.1 (21.2–25.6)
Cai[18]	Shenzhen	China	Hospitalized patients	298	48	48.7	HTN: 15.8, CVD: 8.4, DM: 6.0	BMI: 23.2 (21.1–25.6)
Cai[59]	Shenzhen	China	Hospitalized patients	80	47	43.8	-	BMI: 22.9 (16.2–31.6)
Cai[60]	Shenzhen	China	Hospitalized patients	383	-	47.8	HTN: 15.1, CVD:9.1, DM: 5.7	BMI ≥ 28: 10.7%
Chen[23]	Taizhou	China	Hospitalized patients	145	47.5	54.5	HTN: 15.2, DM: 9.7	BMI (severe): 24.8 (23.1–27.0) BMI (nonseverely): 23.2 (21.7–25.7)
Gao[61]	Wenzhou	China	Patients with/without metabolic associated fatty liver disease	130	46	63.1	HTN: 19.2	BMI: 25.0 ± 3.8 BMI (with fatty liver disease): 26.2 ± 3.9 BMI (without fatty liver disease): 23.7 ± 3.2 BMI ≥ 25: 48.5%
He[62]	Wenzhou	China	Asymptomatic patients	12	31	50	HTN: 0, DM: 0	BMI: 22.4 (20.5–23.1)
Targher[63]	Wenzhou	China	Hospitalized patients	339	-	47.2	HTN: 23.3, DM: 17.4	BMI ≥ 25: 38.4%
Yang[64]	Wenzhou	China	Hospitalized patients	149	45.1	54.3	CVD: 18.8	BMI: 23.8 ± 4.5
Zheng[65]	Wenzhou	China	Patients with metabolic associated fatty liver disease	66	47	74.2	HTN: 28.8, DM: 24.2	BMI: 26.5 ± 3.9 BMI > 25: 68.2%

TABLE A2 (Continued)

Reference (first author)	Region	Country	Population	Case numbers	Mean/median age	Male ratio (%)	Common comorbidities (HTN, CVD, DM) (%)	Descriptions of BMI (median, IQR; mean ± SD) or obesity (%)
Cao[66]	Wuhan	China	Hospitalized patients	102	54	52	HTN: 27.5, CVD: 4.9, DM: 10.8	BMI: 24.4 (21.8–26.0)
Li[19]	Wuhan	China	Hospitalized patients	548	60	50.9	HTN: 30.3, CVD: 6.2, DM: 15.1	BMI: 24.7 (22.4–26.7)
Lin[67]	Wuhan	China	Hospitalized patients	323	61	51.4	HTN: 32.5, CVD: 12.7, DM: 14.6	BMI ≥ 25: 20.1%
Liu[24]	Wuhan	China	Hospitalized health care workers	30	35	33	-	BMI (severe): 22.0 ± 1.3 BMI (nonsevere): 27.0 ± 2.5
Liu[68]	Wuhan	China	Hospitalized patients	245	54	46.5	HTN: 21.2, CVD: 7.4, DM: 9.4	BMI: 23.7 ± 3.3
Peng[25]	Wuhan	China	Hospitalized patients with cardiovascular disease	112	62	47	HTN: 82.1, CVD:55.4, DM: 20.5	BMI: 22 (20–25)
Sun[27]	Wuhan	China	Hospitalized patients	57	-	50.9	-	BMI (severe): 24.0 (21.5–26.0) BMI (nonsevere): 26.8 (23.0–29.9)
Xiong[26]	Wuhan	China	Patients under haemodialysis	131	63.3	57.3	CVD: 68.7, DM: 22.9	BMI: 23.1 ± 4
Zhang[69]	Wuhan	China	Severe or critical patients	20	71.2	55	HTN: 50, CVD: 20, DM: 15	BMI: 24.2 ± 1.8 Obesity: 20%
Pedersen[70]	Roskilde	Denmark	Patients with ventilator support	16	69.5	75	HTN: 56, CVD: 19, DM: 13	BMI: 28.9
Mahévas[71]	France	France	Patients with covid-19 pneumonia who require oxygen	173	60	72	CVD: 51, DM: 9	Obesity: 26%
Simonnet[33]	Lille	France	Hospitalized patients	124	60	73	HTN: 49, DM: 23	BMI: 29.6 (26.4–36.4)
Evrard[72]	Limoges	France	Patients with ARDS under ventilation	18	70	67	HTN: 61, DM: 22	BMI: 29 (26–32)
Caussy[73]	Lyon	France	Severe or critical patients	340	-	58	HTN: 57, CVD: 26, DM: 21	Obesity: 25%
Million[74]	Marseille	France	SARS-CoV-2 tested positive patients	1061	43.6	46.4	HTN: 14, CVD: 4.3, DM: 7.4	Obesity: 5.8%
Dreher[75]	Aachen	Germany	Hospitalized patients	50	65	66	HTN: 70, DM: 58	BMI: 29 (25–31) Obesity: 34%
Itelman[76]	Tel HaShomer	Israel	Hospitalized patients	162	52	64.8	HTN: 30.2, DM: 18.5	BMI: 27.3 (23.9–31.2)
Bellosta[77]	Brescia	Italy	Patients with acute lower extremity ischaemia	20	75	90	HTN: 55, CVD: 10, DM: 15	Obesity: 20%
Inciardi[78]	Brescia	Italy	Hospitalized patients	99	67	81	HTN: 64, CVD:16, DM: 31	Obesity: 23%

(Continues)

TABLE A2 (Continued)

Reference (first author)	Region	Country	Population	Case numbers	Mean/median age	Male ratio (%)	Common comorbidities (HTN, CVD, DM) (%)	Descriptions of BMI (median, IQR; mean ± SD) or obesity (%)
Paderno[79]	Brescia	Italy	SARS-CoV-2 tested positive patients	508	-	56.1	HTN: 32.7, CVD:10.2, DM: 12.8	Obesity: 13.2%
Piva[80]	Brescia	Italy	Severe or critical patients	33	64	91	DM: 6	BMI: 27.8 (27.0–32.1) Obesity: 18%
Bhoori[81]	Milan	Italy	Liver transplant patients	151	-	-	HTN: 91.4, DM: 50.3	BMI > 25: 74.8%
Lodigiani[82]	Milan	Italy	Hospitalized patients	388	66	68	HTN: 47.2, CVD: 13.9, DM: 22.7	Obesity: 24.1%
Mauri[83]	Milan	Italy	Patients with ARDS	10	57	70	HTN: 30	BMI: 29 (25–33) Obesity: 40%
Spiezia[84]	Padua	Italy	Severe or critical patients	22	67	90.9	-	BMI: 30 ± 6
Ihle-Hansen[85]	Viken	Norway	Hospitalized patients	42	72.5	67	DM: 17	BMI ≥ 25: 44%
Cardoso[86]	Lisbon	Portugal	Critically ill patients	20	67	90	-	BMI: 29 (26–32)
Barrasa[87]	Vitoria	Spain	Severe or critical patients	48	63.2	56	HTN: 44, CVD: 10, DM: 19	Obesity: 48%
Docherty[88]	UK	UK	Hospitalized patients	20 133	72.9	59.9	CVD: 30.9, DM: 28.1	Obesity: 10.5%
Lusignan[89]	UK	UK	SARS-CoV-2 tested positive patients	587	-	50.4	HTN: 35.6, CVD: 23.2, DM:19.4	Obesity: 28.6%
Aggarwal[90]	Des Moines	USA	Hospitalized patients	16	67	75	HTN: 57, CVD: 19, DM: 31	Obesity: 50%
Gold[91]	Georgia	USA	Hospitalized patients	305	60	49.5	HTN: 67.5, CVD: 25.6, DM: 39.7	BMI ≥ 40: 12.7%
Eboni[92]	Louisiana	USA	SARS-CoV-2 tested positive patients	3481	54	40	HTN: 30.9, CVD: 4.0, DM: 16.3	Obesity: 49.6%
Mohamed[93]	Louisiana	USA	Hospitalized patients	575	-	54.3	HTN: 73.7, DM: 48.9	BMI (AKI): 34 (16–67) BMI (no AKI): 31 (14–67)
Ketcham[94]	Michigan	USA	Heart transplant recipients	13	61	100	HTN: 85, CVD: 46, DM: 69	BMI: 29 ± 8
Cummings[95]	New York	USA	Critically ill patients	257	62	67	HTN: 63, CVD: 19, DM: 36	Obesity: 46%
Goyal[31]	New York	USA	Hospitalized patients	393	62.2	60.6	HTN: 50.1, CVD: 13.7, DM: 25.2	Obesity: 35.8%
Latif[96]	New York	USA	Recipients of heart transplant	28	64	79	HTN: 71, DM: 61	BMI: 26.0 (23.5–30.7)
Lighter[29]	New York	USA	Hospitalized patients	3615	-	-	-	Obesity: 37.9%
Palaiodimos[97]	New York	USA	Hospitalized patients	200	64	49	HTN: 76, CVD: 16.5, DM: 39.5	BMI: 30 (26–35) BMI ≥ 35: 23%

TABLE A2 (Continued)

Reference (first author)	Region	Country	Population	Case numbers	Mean/median age	Male ratio (%)	Common comorbidities (HTN, CVD, DM) (%)	Descriptions of BMI (median, IQR; mean ± SD) or obesity (%)
Pereira[98]	New York	USA	Solid organ transplant recipients	90	57	59	HTN: 64, DM: 46	BMI > 40: 6%
Petrilli[28]	New York	USA	SARS-CoV-2 tested positive patients	5279	54	49.5	HTN: 42.7, CVD: 52.1, DM: 22.6	Obesity: 35.3%
Richardson[99]	New York	USA	Hospitalized patients	5700	63	60.3	HTN: 56.6, CVD: 11.1, DM: 33.8	Obesity: 41.7%
Kalligeros[32]	Rhode Island	USA	Hospitalized patients	103	60	61.1	HTN: 64, CVD: 24.2, DM: 36.8	Obesity: 47.6%
Bhatraju[30]	Washington	USA	Severe or critical patients	24	64	63	DM: 58	BMI: 33.2 ± 7.2 Obesity: 54.2%
Buckner[100]	Washington	USA	Hospitalized patients	105	69	50	HTN: 59, CVD: 38, DM: 33	Obesity: 47%
Kimball[101]	Washington	USA	Residents of a long-term care facility	23	80.7	30.4	CVD: 87, DM: 39.1	Obesity: 26.1%
Bode[102]	USA	USA	Hospitalized patients	1122	-	55.6	DM: 40.2	BMI (patients with diabetes and/or uncontrolled hyperglycaemia): 31.8 ± 13 BMI (patients without diabetes or uncontrolled hyperglycaemia): 30.8 ± 15
Garg[103]	USA	USA	Hospitalized patients	180	-	-	HTN: 49.7, CVD: 27.8, DM: 28.3	Obesity: 48.3%
Jacobs[104]	USA	USA	Patients treated with ECMO	32	52.4	68.8	DM: 34.3	Obesity: 43.8%

Abbreviations: AKI, acute kidney injury; ARDS, acute respiratory distress syndrome; BMI, body mass index; COVID-19, coronavirus disease 2019; CVD, cardiovascular disease; DM, diabetes mellitus; ECMO, extracorporeal membrane oxygenation; HTN, hypertension; IQR, interquartile range.