Overweight and Obesity are Risk Factors of Severe Illness in Patients with COVID-19

Jian Wang1*, Li Zhu2*, Longgen Liu3*, Xiang-an Zhao4*, Zhaoping Zhang1*, Leyang Xue5*, Xuebing Yan6, Songping Huang7, Yang Li8, Juan Cheng9, Biao Zhang10, Tianmin Xu11, Chunyang Li12, Fang Ji13, Fang Ming14, Yun Zhao15, Huaping Shao16, Dawen Sang9, Haiyan Zhao12, Xinying Guan13, Xiaobing Chen14, Yuxin Chen15, Rahma Issa16, Jie Wei16, Rui Huang1, Chuanwu Zhu2, and Chao Wu1

Objective: This study aimed to observe the clinical characteristics of patients with coronavirus disease 2019 (COVID-19) with overweight and obesity.

Methods: Consecutive patients with COVID-19 from 10 hospitals of Jiangsu province, China, were enrolled.

Results: A total of 297 patients with COVID-19 were included, and 39.39% and 13.47% of patients had overweight and obesity, respectively. The proportions of bilateral pneumonia (92.50% vs. 73.57%, P = 0.033) and type 2 diabetes (17.50% vs. 3.57%, P = 0.006) were higher in patients with obesity than lean patients. The proportions of severe illness in patients with obesity (12.82% vs. 2.86%, P = 0.006) and obesity (25.00% vs. 2.86%, P < 0.001) were significantly higher than lean patients. More patients with obesity developed respiratory failure (20.00% vs. 2.86%, P < 0.001) and acute respiratory distress syndrome (5.00% vs. 0%, P = 0.024) than lean patients. The median days of hospitalization were longer in patients with obesity than lean patients (17.00 days vs. 14.00 days, P = 0.029). Overweight (OR, 4.222; 95% CI: 1.322-13.476; P = 0.015) and obesity (OR, 9.216; 95% CI: 2.581-32.903; P = 0.001) were independent risk factors of severe illness. Obesity (HR, 6.607; 95% CI: 1.955-22.329; P = 0.002) was an independent risk factor of respiratory failure.

Conclusions: Overweight and obesity were independent risk factors of severe illness in COVID-19 patients. More attention should be paid to these patients.

Obesity (2020) 28, 2049-2055.

Introduction

Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was declared a pandemic by the World Health Organization (1). Although most of the SARS-CoV-2 infection typically leads to relatively mild symptoms, 287,399 patients still died globally up to May 13, 2020 (2). Old age and comorbidities, such as hypertension, diabetes, and chronic respiratory disease, were identified as risk factors of poor outcomes for patients with COVID-19 according to previous studies (3,4). Obesity was regarded as a common risk factor to aggravate the severity of respiratory diseases, which was associated with poor prognosis in influenza A pulmonary infection (5,6). Animal experiments have found that obesity alters inflammatory and pathological responses in the lung during influenza (7-9). Excessive adipose accumulation could result in insulin resistance, oxidative stress, chronic inflammation, and circulating nutrients abnormality (10,11). However, few studies have focused on the impacts of obesity on COVID-19.

A retrospective study that enrolled 124 patients with COVID-19 who were admitted to intensive care unit (ICU) showed more patients required invasive mechanical ventilation (IMV) therapy with increased BMI (12). Another study found that patients with COVID-19 who were aged<60 years with a BMI between 30 and 34 kg/m² had 2.0 and 1.8 times the...
risk for admission to acute and critical care as compared with individuals with a BMI <30 kg/m^2, respectively (13). These studies suggested that obesity may be associated with the severity of COVID-19. However, for several confounders such as age, the presence of comorbidities were not adjusted, which might have impacted the results. Whether overweight and obesity are independent risk factors of severe COVID-19 requires further research. In addition, the sample sizes are relatively small in the previous studies (12,13). This study aimed to investigate the clinical features of patients with COVID-19 with overweight and obesity in a multicenter cohort of COVID-19 in Jiangsu province, China.

**Methods**

**Study population**

Between January 18, 2020, and February 26, 2020, 342 consecutive patients with COVID-19 from 10 medical centers in 10 cities of Jiangsu, China, were enrolled. All patients with COVID-19 were diagnosed by clinical manifestations, chest computed tomography, and real-time polymerase chain reaction according to World Health Organization interim guidance and the Guidelines for the Diagnosis and Treatment of Novel Coronavirus Infection by the National Health Commission (Trial Version 5) (14,15). All patients with COVID-19 were tested positive for SARS-CoV-2 by real-time polymerase chain reaction in throat swab specimens. The last followed-up date was February 29, 2020. The study was approved by the ethics review boards of these medical centers.

**Data collection and study definitions**

We retrospectively recorded the clinical characteristics, complications, and outcomes of patients by electronic medical record system. The computational formula of BMI was weight (kilograms) divided by height (meters) squared. According to criterion of guidelines for prevention and control of overweight and obesity in Chinese adults, 24 ≤ BMI <28 and BMI ≥ 28 was defined as overweight and obesity, respectively (16,17). Severe COVID-19 was defined according to the current guideline as follows: (1) respiratory frequency ≥ 30/min, (2) pulse oximeter oxygen saturation ≤ 93% at rest, and (3) oxygenation index ≤ 300 mmHg (15). Acute respiratory distress syndrome (ARDS) was defined according to the Berlin definition (18).

**Statistical analysis**

Continuous variables were described as medians (interquartile range [IQR]), and categorical variables were presented as the counts and percentages. The independent group t tests (normal distribution) and Mann-Whitney U (non-normal distribution) were used to compared continuous variables between groups. Chi-square or Fisher exact test was used to compare the categorical variables. Multivariate logistic and cox regression analysis was used to adjust for confounding factors, including age, gender, and comorbidities. P < 0.05 was considered to be statistically significant. SPSS version 22.0 software (SPSS Inc., Chicago, Illinois) was used for the analysis.

**Results**

**Clinical characteristics of patients with overweight and obesity on admission**

Thirty-four patients were excluded because of the lack of BMI data, and 11 patients under 12 years old were also excluded. Eventually, 297 patients were enrolled in this study. The clinical characteristics were presented in Table 1. Of the 297 patients with COVID-19, 117 (39.39%) and 40 (13.47%) had overweight (24 ≤ BMI <28) and obesity (BMI ≥ 28), respectively. The median age was 38.00 (IQR, 31.25-54.00) years, 48.00 (IQR, 36.50-57.00) years, and 47.00 (IQR, 34.25-57.75) years in patients with lean (BMI <24), overweight, and obesity, respectively. Patients with overweight and obesity were older, and the proportion of male gender was higher in patients with overweight and obesity than lean patients. The median BMI was 22.17 (IQR, 20.55-23.12), 25.71 (IQR, 24.87-26.61), and 29.75 (IQR, 29.18-30.81) in these three groups, respectively. The proportions of a medical history of type 2 diabetes were significantly different in these three groups (P = 0.008). More patients had a history of type 2 diabetes in the obesity group than the lean group (17.50% vs. 3.57%, P = 0.006), whereas the proportion was comparable between the overweight group and lean group (11.11% vs. 3.57%, P = 0.054). The clinical symptoms on admission were similar among the three groups. The median levels of fasting blood glucose (FBG) presented an increasing trend in patients who were lean and with overweight and obesity (P < 0.001). Patients with obesity presented higher FBG levels than lean patients (6.48 mmol/L vs. 5.47 mmol/L, P < 0.001), whereas patients with overweight had similar FBG levels with lean patients (5.69 mmol/L vs. 5.47 mmol/L, P = 0.119). However, there were no significant differences in triglycerides and total cholesterol among the three groups. The proportion of bilateral pneumonia presented an increasing trend in patients who were lean and with overweight and obesity (P = 0.018). More patients with obesity had bilateral pneumonia on admission than lean patients (92.50% vs. 73.57%, P = 0.033), while there was no difference between patients with overweight and lean patients (82.91% vs. 73.57%, P = 0.219).

**Treatment and clinical outcomes of patients with overweight and obesity**

The proportions of patients who used atomized inhalation of interferon α-2b (60.00%, 56.41%, and 57.50%, P = 0.84), lopinavir-ritonavir (70.01%, 75.21%, and 80.00%, P = 0.383), and arbidol (52.86%, 47.86%, and 52.50%, P = 0.709) were comparable among the three groups (Table 2). The proportions of oxygen therapy (P = 0.009) and non-IMV therapy (P = 0.003) were significantly different in these three groups. More patients with overweight received oxygen therapy compared with lean patients (66.67% vs. 48.57%, P = 0.012) during hospitalization, while the proportion of oxygen therapy was comparable between patients with obesity and lean patients (65.00% vs. 48.57%, P = 0.201). Moreover, more patients with overweight (6.84% vs. 0.71, P = 0.024) and obesity (12.50% vs. 0.71, P < 0.001) received non-IMV therapy than lean patients. No patient received IMV treatment in our study. The proportions of patients who developed respiratory failure (P = 0.001) and ARDS (P = 0.049) were significantly different in these three groups. In total, 20% of patients with obesity developed respiratory failure, which was significantly higher than in lean patients (2.86%, P < 0.001), while the proportion of respiratory failure was comparable between patients with overweight and lean patients (8.55% vs. 2.86%, P = 0.135). Similarly, the proportions of patients developing ARDS were higher in patients with obesity than lean patients (5.00% vs. 0%, P = 0.024), while the proportion of ARDS was comparable between patients with overweight and lean patients (1.71% vs. 0%, P = 0.360). The proportions of severe illness were different in the three groups (P < 0.001). More patients with overweight (12.82% vs. 2.86%, P = 0.006) and obesity (25.00% vs. 2.86%, P < 0.001) had severe illness than lean patients. However, the proportions of patients admitted to ICU were comparable among the three groups (P = 0.087). The median days of hospitalization were different among the three groups (P = 0.025). Patients
with obesity stayed longer in hospital than lean patients (17.00 days vs. 14.00 days, \(P = 0.029\)), while there was no significant difference of hospital stays between patients with overweight and lean patients (16.00 days vs. 14.00 days, \(P = 0.421\)).

The distributions of BMI categories were significantly different between patients with severe illness and nonsevere illness (\(P < 0.001\)), respiratory failure and nonrespiratory failure (\(P = 0.001\)), noninvasive mechanical ventilation and without noninvasive mechanical ventilation (\(P = 0.003\)) (Figure 1). However, although the proportions of patients with overweight and obesity had a higher rate of ICU admission, the difference was not statistically significant (\(P = 0.087\)).

### Associations of overweight and obesity with severe illness

Logistic regression analysis was performed to identify the association between obesity and severe illness (Table 3). Univariate analysis presented that overweight (odds ratio \([OR]\), 5.000; 95% CI: 1.611-15.516; \(P = 0.005\)), obesity (OR, 11.333; 95% CI: 3.329-38.583; \(P < 0.001\)), and type 2 diabetes (OR, 7.087; 95% CI: 2.782-18.053; \(P < 0.001\)) were associated with severe illness. In the multivariate analysis, overweight (OR, 4.222; 95% CI: 1.322-13.476; \(P = 0.015\)) and obesity (OR, 9.216; 95% CI: 2.581-32.903; \(P = 0.001\)) were independent risk factors of severe COVID-19 after adjusted age, sex, the presence of hypertension, and type 2 diabetes.

### Associations of overweight and obesity with respiratory failure

The associated factors of respiratory failure in patients with COVID-19 were analyzed by cox regression analysis (Table 4). The univariate analysis showed that the factors for respiratory failure were obesity (HR, 7.542; 95% CI: 2.270-25.055; \(P = 0.001\)) and type 2 diabetes (HR, 4.986; 95% CI: 1.949-12.756; \(P = 0.001\)). On multivariate analysis,
Obesity and Obesity in COVID-19 Patients Wang et al.

Overweight and Obesity in COVID-19 Patients

Wang et al.

obesity (HR, 6.607; 95% CI: 1.955-22.329; \( P = 0.002 \)), type 2 diabetes (HR, 5.197; 95% CI: 1.837-14.699; \( P = 0.002 \)), and age > 60 years (HR, 2.766; 95% CI: 1.018-7.514; \( P = 0.046 \)) were associated with an increased risk of respiratory failure.

Discussion

Overweight and obesity are serious global health problems (19,20). The global prevalence ratios of overweight and obesity are 38.5% to
Obesity

After adjusting the confounding factors such as age and sex, overweight and obesity were still independent risk factors of severe illness of COVID-19. Taken together, these results suggested that overweight and obesity were independently associated with the severity of COVID-19.

However, the mechanisms of overweight and obesity contributing to severe COVID-19 are not yet defined. Obesity has been regarded as a risk factor of severe illness and poor prognosis in many infectious diseases (28). Obesity induces systematically chronic inflammation by increasing the secretion of cytokines such as interleukin 6, interleukin 8, and tumor necrosis factor-α, which may aggravate the injury of lung parenchyma and bronchi (29-31). A previous study has also found that obesity might impair adaptive immune responses in influenza virus infection (32). A similar mechanism might exist in patients with COVID-19. In addition, obesity causes a decrease in protective cardiorespiratory reserve and immune dysfunction (33). Sattar et al. (33) also reported obesity could increase the risk of thrombosis, which is an unignorable risk factor of severe COVID-19. With regard to lung function, obesity reduces expiratory volume and forced vital capacity (33-35). In addition, animal models demonstrated that obesity leads to decreased natural killer cell cytotoxicity and increased mortality in influenza infection (36). However, the mechanisms of overweight and obesity in the severity of COVID-19 deserve further investigation.

### TABLE 3 Logistic regression analysis of risk factors for patients with severe COVID-19

| Variables                      | Univariate          | Multivariate         |
|-------------------------------|---------------------|----------------------|
|                               | OR (95% CI)         | P        | OR (95% CI) | P        |
| Age                           |                     |          |             |          |
| ≤ 60                          | Reference           |          |             |          |
| > 60                          | 1.577 (0.635-3.913) | 0.326   | 1.410 (0.469-4.244) | 0.541   |
| Sites                         |                     |          |             |          |
| 1.023 (0.897-1.190)           | 0.770   |          | 1.925 (0.729-5.088) | 0.186   |
| Sex                           |                     |          |             |          |
| Female                        | Reference           |          |             |          |
| Male                          | 2.295 (0.982-5.363) | 0.055   | 4.167 (1.296-13.402) | 0.017   |
| BMI (kg/m²)                   |                     |          |             |          |
| < 24                          | Reference           |          |             |          |
| 24-28                         | 5.000 (1.611-15.516) | 0.005 | 9.028 (2.523-32.299) | 0.001 |
| ≥ 28                          | 11.333 (3.329-38.583) | <0.001 |             |          |
| Hypertension                  |                     |          |             |          |
| No                            | Reference           |          |             |          |
| Yes                           | 1.090 (0.394-3.015) | 0.868   | 0.435 (0.124-1.528) | 0.194   |
| Type 2 diabetes               |                     |          |             |          |
| No                            | Reference           |          |             |          |
| Yes                           | 7.087 (2.782-18.053) | <0.001 | 5.333 (1.800-15.800) | 0.003   |
| Chronic lung diseases         |                     |          |             |          |
| No                            | Reference           |          |             |          |
| Yes                           | 1.911 (0.398-9.178) | 0.418   | 1.751 (0.322-9.511) | 0.517   |
| Cardiovascular diseases       |                     |          |             |          |
| No                            | Reference           |          |             |          |
| Yes                           | 1.879 (0.212-16.653) | 0.571   | 0.968 (0.066-14.280) | 0.981   |
| Malignant tumors              |                     |          |             |          |
| No                            | Reference           |          |             |          |
| Yes                           | 3.155 (0.317-31.354) | 0.327 | 1.768 (0.150-20.879) | 0.651   |

OR, odds ratio.
There were several limitations in our study. First, the outcomes of patients with COVID-19 had relatively favorable outcomes with no deaths. Thus, we could not analyze the association of overweight/obesity and fatal outcome in patients with COVID-19. Second, the associations of overweight/obesity with IMV could not be analyzed either. However, Kalligeros et al. (37) reported the potential association of obesity with severe outcomes in 102 patients hospitalized with COVID-19. They found that obesity was independently associated with the use of IMV (37). Third, many of the treatments and outcomes (oxygen therapy, non-IMV, admission to ICU, days of hospitalization) are subject to bias from clinicians who were in charge for the management of patients. Fourth, our study was conducted later in the pandemic, and by this point, people had suspicions and some studies were already conducted on the topic that overweight and obesity were risk factors for more severe COVID-19 outcomes. Thus, the clinicians in charge of care might have just been overly cautious, which might have biased our results. Furthermore, we could not include all the patients in our province. Thus, there is a potential selection bias in our study. However, nearly half of the confirmed cases in our province were included in our present study. We consider that our study is representative. Finally, the impacts of overweight and obesity on the long-term outcomes of patients with COVID-19 remain unclear.

In conclusion, patients with COVID-19 with overweight and obesity had higher risks for severe illness. Therefore, more attention should be paid to patients with COVID-19 with overweight or obesity. However, more studies are needed to confirm our findings and to reveal the underlying mechanisms of overweight and obesity associated with higher risks for severe illness in COVID-19.

Funding agencies: This study was supported by the Fundamental Research Funds for the Central Universities (No. 14380459).

Disclosure: The authors declared no conflict of interest exist.

Author contributions: Concept and design: CW, RH, and CZ; drafting of the manuscript: JWang, RH, and XZ; critical revision of the manuscript for important intellectual content: CW, RH, LX, LL, ZZ, RI, and CZ; statistical analysis: JWang; administrative, technical, or material support: LZ, XZ, ZZ, XY, SH, JC, BZ, TX, CL, FJ, FM, YZ, HS, DS, HZ, XG, XC, and YC; supervision: CW; acquisition, analysis, or interpretation of data: JWei, LZ, LL, XZ, ZZ, and RH. All authors reviewed and approved the final version.

References
1. World Health Organization. WHO characterizes COVID-19 as a pandemic. Rolling updates on coronavirus disease (COVID-19) website. https://www.who.int/emergencies/ diseases/novel-coronavirus-2019/events-as-they-happen. Published March 11, 2020. Updated July 31, 2020. Accessed March 15, 2020.
2. World Health Organization. Coronavirus disease 2019 (COVID-19) Situation Report – 55. https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200315sitrep-55-covid-19.pdf?sfvrsn=33da5cb_8. Published March 15, 2020. Accessed March 15, 2020.
3. Guan WJ, Ni ZY, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 2020;382:1708-1720.
4. Chen T, Wu D, Chen H, et al. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. BMJ 2020;368:m1091. doi:10.1136/bmj.m1091

There were several limitations in our study. First, the outcomes of patients with COVID-19 had relatively favorable outcomes with no deaths. Thus, we could not analyze the association of overweight/obesity and fatal outcome in patients with COVID-19. Second, the associations of overweight/obesity with IMV could not be analyzed either. However, Kalligeros et al. (37) reported the potential association of obesity with severe outcomes in 102 patients hospitalized with COVID-19. They found that obesity was independently associated with the use of IMV (37). Third, many of the treatments and outcomes (oxygen therapy, non-IMV, admission to ICU, days of hospitalization) are subject to bias from clinicians who were in charge for the management of patients. Fourth, our study was conducted later in the pandemic, and by this point, people had suspicions and some studies were already conducted on the topic that overweight and obesity were risk factors for more severe COVID-19 outcomes. Thus, the clinicians in charge of care might have just been overly cautious, which might have biased our results. Furthermore, we could not include all the patients in our province. Thus, there is a potential selection bias in our study. However, nearly half of the confirmed cases in our province were included in our present study. We consider that our study is representative. Finally, the impacts of overweight and obesity on the long-term outcomes of patients with COVID-19 remain unclear.

In conclusion, patients with COVID-19 with overweight and obesity had higher risks for severe illness. Therefore, more attention should be paid to patients with COVID-19 with overweight or obesity. However, more studies are needed to confirm our findings and to reveal the underlying mechanisms of overweight and obesity associated with higher risks for severe illness in COVID-19.

Funding agencies: This study was supported by the Fundamental Research Funds for the Central Universities (No. 14380459).

Disclosure: The authors declared no conflict of interest exist.

Author contributions: Concept and design: CW, RH, and CZ; drafting of the manuscript: JWang, RH, and XZ; critical revision of the manuscript for important intellectual content: CW, RH, LX, LL, ZZ, RI, and CZ; statistical analysis: JWang; administrative, technical, or material support: LZ, XZ, ZZ, XY, SH, JC, BZ, TX, CL, FJ, FM, YZ, HS, DS, HZ, XG, XC, and YC; supervision: CW; acquisition, analysis, or interpretation of data: JWei, LZ, LL, XZ, ZZ, and RH. All authors reviewed and approved the final version.

References
1. World Health Organization. WHO characterizes COVID-19 as a pandemic. Rolling updates on coronavirus disease (COVID-19) website. https://www.who.int/emergencies/ diseases/novel-coronavirus-2019/events-as-they-happen. Published March 11, 2020. Updated July 31, 2020. Accessed March 15, 2020.
2. World Health Organization. Coronavirus disease 2019 (COVID-19) Situation Report – 55. https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200315sitrep-55-covid-19.pdf?sfvrsn=33da5cb_8. Published March 15, 2020. Accessed March 15, 2020.
3. Guan WJ, Ni ZY, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 2020;382:1708-1720.
4. Chen T, Wu D, Chen H, et al. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. BMJ 2020;368:m1091. doi:10.1136/bmj.m1091

TABLE 4 Cox regression analysis of risk factors for respiratory failure

| Variables                  | Univariate       | Multivariate      |
|---------------------------|------------------|-------------------|
|                           | HR (95% CI)  | P     | HR (95% CI) | P     |
| Age ≤ 60                  | Reference       |       |                |       |
| Age > 60                  | 1.927 (0.754-4.926) | 0.170 | 2.766 (1.018-7.514) | 0.046 |
| Sex Female                | Reference       |       |                |       |
| Sex Male                  | 1.808 (0.737-4.434) | 0.196 | 1.432 (0.537-3.824) | 0.473 |
| BMI (kg/m²) < 24          | Reference       |       |                |       |
| BMI (kg/m²) 24-28         | 2.969 (0.931-9.467) | 0.066 | 2.349 (0.708-7.798) | 0.163 |
| BMI (kg/m²) ≥ 28          | 7.542 (2.270-25.055) | 0.001 | 6.607 (1.955-22.329) | 0.002 |
| Hypertension No           | Reference       |       |                |       |
| Hypertension Yes          | 0.803 (0.238-2.713) | 0.724 | 0.359 (0.092-1.400) | 0.140 |
| Type 2 diabetes No        | Reference       |       |                |       |
| Type 2 diabetes Yes       | 4.986 (1.949-12.756) | 0.001 | 5.197 (1.837-14.699) | 0.002 |
| Chronic lung diseases No  | Reference       |       |                |       |
| Chronic lung diseases Yes | 2.446 (0.572-10.467) | 0.228 | 2.233 (0.489-10.198) | 0.300 |
| Cardiovascular diseases No| Reference       |       |                |       |
| Cardiovascular diseases Yes| 0.048 (0.000-15003.613) | 0.638 | 0.981 |
| Malignant tumors No       | Reference       |       |                |       |
| Malignant tumors Yes      | 3.741 (0.503-27.835) | 0.198 | 2.319 (0.285-18.878) | 0.432 |

OR, odds ratio.
5. Milner JJ, Rebeles J, Dhungana S, et al. Obesity increases mortality and modulates the lung metabolome during pandemic H1N1 influenza virus infection in mice. *J Immunol* 2015;194:4846-4859.

6. Bijani B, Pahlevan AA, Qasemi-Barqi R, Jahanhashemi H. Metabolic syndrome as an independent risk factor of hypoxemia in influenza A (H1N1) 2009 pandemic. *Infect Med* 2016;24:123-130.

7. O’Brien KB, Vogel P, Duan S, et al. Impaired wound healing predisposes obese mice to severe influenza virus infection. *J Infect Dis* 2012;205:252-261.

8. Karlsson EA, Sheridan PA, Beck MA. Diet-induced obesity impairs the T cell memory response to influenza virus infection. *J Immunol* 2010;184:3127-3133.

9. Milner JJ, Sheridan PA, Karlsson EA, Schultz-Cherry S, Shi Q, Beck MA. Diet-induced obese mice exhibit altered heterologous immunity during a secondary 2009 pandemic H1N1 infection. *J Immunol* 2013;191:2474-2485.

10. Milner JJ, Beck MA. The impact of obesity on the immune response to infection. *Proc Nutr Soc* 2012;71:295-306.

11. Johnson AR, Milner JJ, Makowski L. The inflammation highway: metabolism accelerates inflammatory traffic in obesity. *Infect Immun* 2012;80:218-238.

12. Simonnet A, Chatboun M, Poissy J, et al. High prevalence of obesity in severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) requiring invasive mechanical ventilation. *Obesity (Silver Spring)* 2020;28:1195-1199.

13. Lighter J, Phillips M, Hochman S, et al. Obesity in patients younger than 60 years is a risk factor for Covid-19 hospital admission. *Clin Infect Dis* 2020;71:896-897.

14. World Health Organization. Clinical management of COVID-19. https://www.who.int/publications/i/item/clinical-management-of-covid-19. Accessed February 8, 2020.

15. National Health Commission of the People’s Republic of China. Diagnosis and Treatment Protocol for COVID-19 (Trial Version 7). http://en.nhc.gov.cn/2020-publications/i/item/clinical-management-of-covid-19. Accessed February 8, 2020.

16. Zhao S, Jia X, Fan X, et al. Association of obesity with the clinicopathological features of thyroid cancer in a large, operative population: a retrospective case-control study. *Obesity (Lond)* 2013;12:373-376.

17. Wang L, Du X, Dong JZ, et al. Body mass index and all-cause mortality in patients with atrial fibrillation: insights from the China atrial fibrillation registry study. *Circulation* 2020;142:4-6.

18. Soto GJ, Frank AJ, Christiani DC, Gong MN. Body mass index and acute kidney injury in the acute respiratory distress syndrome. *Crit Care Med* 2020;48:543-551. doi:10.1007/s15010-020-04325-5

19. Huang I, Lim MA, Pranata R. Diabetes mellitus is associated with increased mortality and severity of disease in COVID-19 pneumonia - a systematic review, meta-analysis, and meta-regression. *Diabetes Metab Syndr: Cardiovasc Dis* 2020;14:395-403.

20. Cui Q, Chen F, Luo F, et al. Obesity and COVID-19 severity in a designated hospital in Shenzhen, China. *Diabetes Care* 2020;43:1392-1398.

21. Zhang X, Zhang J, Zhang L, et al. Systemic inflammation mediates the detrimental effects of obesity on asthma control. *Allergy Asthma Proc* 2018;39:43-50.

22. Soto GJ, Frank AJ, Christiante DC, Gong MN. Body mass index and acute kidney injury in the acute respiratory distress syndrome. *Crit Care Med* 2012;40:2601-2608.

23. Huang I, Lim MA, Pranata R. Diabetes mellitus is associated with increased mortality and severity of disease in COVID-19 pneumonia - a systematic review, meta-analysis, and meta-regression. *Diabetes Metab Syndr: Cardiovasc Dis* 2020;14:395-403.

24. Cui Q, Chen F, Luo F, et al. Obesity and COVID-19 severity in a designated hospital in Shenzhen, China. *Diabetes Care* 2020;43:1392-1398.

25. Huang C, Wang Y, Li X, et al. Clinical characteristics of 145 patients with coronavirus disease 2019 (COVID-19) in Taizhou, Zhejiang, China. *Infection* 2020;48:543-551. doi:10.1007/s15010-020-04325-5

26. Huang I, Lim MA, Pranata R. Diabetes mellitus is associated with increased mortality and severity of disease in COVID-19 pneumonia - a systematic review, meta-analysis, and meta-regression. *Diabetes Metab Syndr: Cardiovasc Dis* 2020;14:395-403.

27. Huang C, Wang Y, Li X, et al. Clinical characteristics of 145 patients with coronavirus disease 2019 (COVID-19) in Taizhou, Zhejiang, China. *Infection* 2020;48:543-551. doi:10.1007/s15010-020-04325-5

28. Huttunen R, Syrjänen J. Obesity and the risk and outcome of infection. *Int J Obes* (Lond) 2013;37:333-340.

29. Zhang X, Zhang J, Zhang L, et al. Systemic inflammation mediates the detrimental effects of obesity on asthma control. *Allergy Asthma Proc* 2018;39:43-50.

30. Soto GJ, Frank AJ, Christiante DC, Gong MN. Body mass index and acute kidney injury in the acute respiratory distress syndrome. *Crit Care Med* 2012;40:2601-2608.

31. Bermejo-Martin JF, Ortiz de Lejarazu R, Pumarola T, et al. Th1 and Th17 hypercytokinemia as early host response signature in severe pandemic influenza. *Crit Care* 2009;13:R201. doi:10.1186/cc8208

32. Green WD, Beck MA. Obesity impairs the adaptive immune response to influenza virus. *Am J Respir Crit Care Med* 2017;196:s406-S409.

33. Sattar N, McInnes IB, McMurray JI. Obesity: a risk factor for severe COVID-19 infection: multiple potential mechanisms. *Circulation* 2020;142:4-6.

34. Watson RA, Pride NB, Thomas EL, et al. Reduction of total lung capacity in obese men: comparison of total intrathoracic and gas volumes. *J Appl Physiol* 2010;108:1605-1612.

35. Jones RL, Nzekwu M-MU. The effects of body mass index on lung volumes. *Chest* 2020;157:854-860. doi:10.1016/j.chest.2019.09.048

36. Delghani M, Akhtar-Danesh N, Merchant AT. Childhood obesity, prevalence and prevention. *Nutr J* 2005;4:24. doi:10.1186/1475-2891-4-24

37. Hossain P, Kawar B, El Nahas M. Obesity and diabetes in the developing world—a growing challenge. *N Engl J Med* 2007;356:213-215.