Obesity Is a Risk Factor for Greater COVID-19 Severity

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The coronavirus disease 2019 (COVID-19) pandemic, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has attracted increasing worldwide attention (1). Obesity commonly aggravates the severity of respiratory diseases, but it is currently not known whether obese patients are also more likely to have greater COVID-19 severity of illness. We investigated the association between obesity and COVID-19 severity of illness among patients with laboratory-confirmed SARS-CoV-2 infection.

We enrolled adult patients with COVID-19 from three hospitals in China between 17 January 2020 and 11 February 2020. Seventy-five patients were diagnosed as obese (i.e., case subjects). We randomly matched each case subject with one control subject (nonobese) by sex (1:1) and age ($\pm$ 5 years). The cohort thus comprised 150 patients with COVID-19. The study protocol was approved by local ethics committees of the three hospitals. The requirement for written informed consent was waived due to the retrospective and anonymous nature of the study.

COVID-19 was diagnosed as a positive result by high-throughput sequencing or real-time reverse transcriptase PCR assay of oropharyngeal swab specimens. COVID-19 severity of illness was assessed during hospitalization and classified into four clinical subtypes (i.e., mild, moderate, severe, or critically ill) based on management guidelines (2). Obesity was defined as BMI ≥ 25 kg/m^2 in this Asian population. Diabetes was determined as either history of diagnosed diabetes, use of antidiabetic drugs, or, in few cases, newly diagnosed diabetes after recovery from acute SARS-CoV-2 infection. Diagnosis of diabetes was made using standard procedures at the three hospitals, based on guidelines of the China Diabetes Society (3). Hypertension and dyslipidemia were diagnosed based on established criteria. All patients denied a history of active cancer, chronic obstructive or restrictive pulmonary diseases, or other end-stage diseases. Patients received standard treatments according to the Chinese COVID-19 management guidance (7th edition) (2) and were all discharged alive from the hospital.

For statistical purposes, COVID-19 patients were categorized into two groups according to their disease severity as nonsevere (i.e., mild and moderate disease, combined) and severe (severe and critical, combined) (2). The association between presence of obesity or increasing BMI values (as exposure measures) and COVID-19 severity (as the outcome measure) was assessed by binary logistic regression analysis. Statistical analyses were two-sided, and significance was set at $P < 0.05$.

The mean age of patients was 48 years, and 62.7% were male. Twenty-nine patients (19.3%) had diabetes; obese patients were more likely to have diabetes than those without obesity

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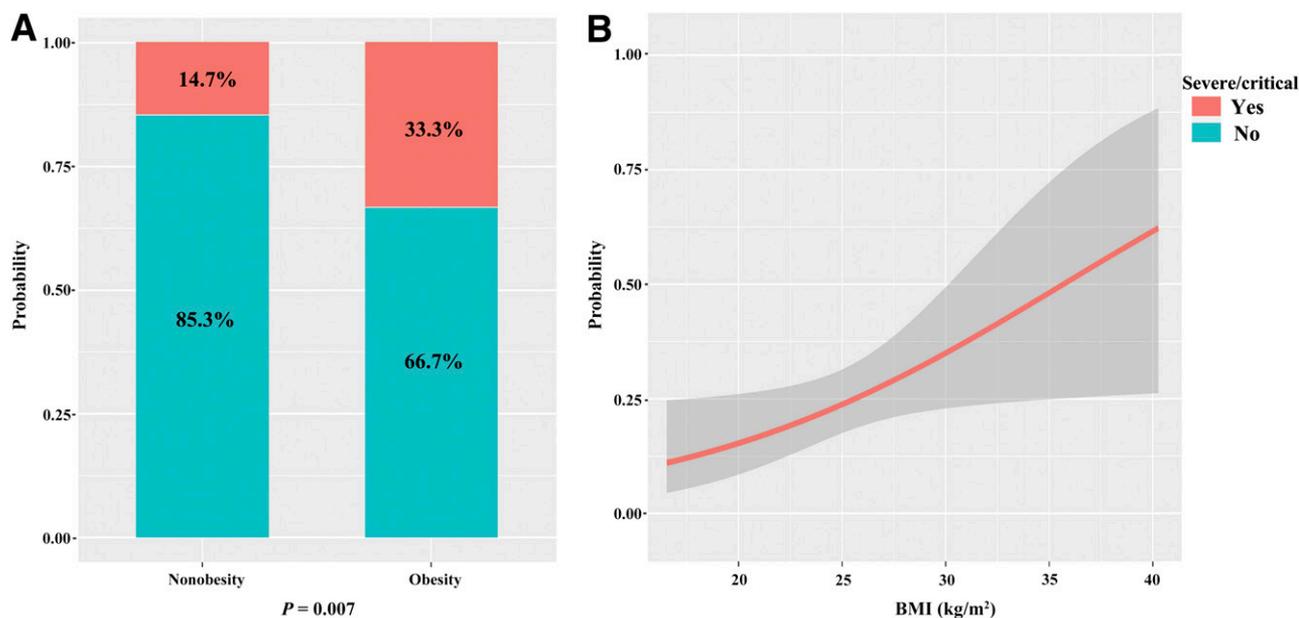
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Figure 1—*A*: Prevalence of clinical subtypes of COVID-19 severity among infected patients with and without obesity. *B*: Association between increasing BMI values and COVID-19 severity.

(24.0% vs. 14.7%). Mean BMI for non-obese and obese patients was 21.8 ± 2.3 and 27.7 ± 2.7 kg/m^2, respectively. At their hospital admission, obese patients had higher levels of plasma C-reactive protein and lower lymphocyte counts, which are considered two early indicators of severe COVID-19 (2). Notably, obese patients also had a longer hospital stay (median 23 [interquartile range 17–30] vs. 18 [13–24] days; $P = 0.037$) and a greater proportion had severe COVID-19 (33.3% vs. 14.7%, $P = 0.007$ by χ^2 test) (Fig. 1*A*) compared with non-obese patients. As shown in Fig. 1*B*, there was a clear dose-effect relationship between increasing values of BMI and the proportion of patients with severe COVID-19.

In the logistic regression analyses, the presence of obesity was associated with an approximately threefold increased risk of having severe COVID-19 (unadjusted odds ratio [OR] 2.91, 95% CI 1.31–6.47). Each 1-unit increase in BMI was also associated with a 12% increase in the risk of severe COVID-19 (unadjusted OR 1.12, 95% CI 1.01–1.23). Notably, the association between obesity (or increasing BMI values) and greater COVID-19 severity remained significant even after adjusting for age, sex, smoking status, hypertension, diabetes, and dyslipidemia (adjusted OR 3.00, 95% CI 1.22–7.38

for obesity, and adjusted OR 1.13, 95% CI 1.01–1.28 for BMI, respectively).

To date, the virologic and physiological mechanisms underlying the strong relationship we observed between obesity and COVID-19 severity are poorly understood. It is plausible to hypothesize that more severe COVID-19 in patients with obesity may be the consequence of underlying low-grade chronic inflammation, and suppression of innate and adaptive immune responses (4). In addition, the altered microenvironment associated with obesity may support a more diverse viral quasispecies and afford the emergence of potentially pathogenic variants capable of inducing greater disease severity (5). Finally, mechanical dysfunction due to severe obesity may increase the severity of lower respiratory tract infection and contribute to secondary infection (6).

Health care professionals caring for COVID-19 patients should be cognizant of the increased likelihood of severe COVID-19 in obese patients. In particular, the presence of obesity increases the risk of severe illness approximately threefold with a consequent longer hospital stay.

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