



# Obesity and impaired metabolic health in patients with COVID-19

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Preliminary data suggest that people with obesity are at increased risk of severe COVID-19. However, as data on metabolic parameters (such as BMI and levels of glucose and insulin) in patients with COVID-19 are scarce, increased reporting is needed to improve our understanding of COVID-19 and the care of affected patients.

In China, older age ( $\geq 65$  years) and the presence of comorbidities are associated with a more severe course of COVID-19 in patients infected with the novel coronavirus (SARS-CoV-2). Among the comorbid conditions, the highest fatality rate was found for cardiovascular disease (CVD) (10.5%) and diabetes mellitus (7.3%), followed by chronic respiratory diseases (6.3%), hypertension (6.0%) and cancer (5.6%)<sup>1</sup>. A direct endocrine and metabolic link between hypertension and diabetes mellitus and coronavirus infection, which might involve angiotensin-converting enzyme 2, is being discussed<sup>2</sup>.

## Early data

Studies from China<sup>1</sup> and the Lombardy region of Italy<sup>3</sup> that have reported comorbidities in patients with COVID-19 did not provide data on body weight and height, which are used to estimate adipose tissue mass by calculating the BMI. A descriptive study of a small sample of 24 (63% were men) critically ill patients diagnosed with COVID-19 in the Seattle region was among the first to report BMI data (3 patients with a BMI in the normal category, 7 with overweight, 13 with obesity and 1 with missing data). Although the numbers are too small for meaningful statistical analyses, 85% of the patients with obesity required mechanical ventilation and 62% of the patients with obesity died. These proportions are greater than those in the patients without obesity, in which 64% required mechanical ventilation and 36% died<sup>4</sup>. As CVD and diabetes mellitus are strongly associated with elevated adipose tissue mass<sup>5</sup>, a high BMI might be an important risk factor for a severe course of disease, particularly of pneumonia, in these patients.

Concern about the effects of BMI is further substantiated by preliminary data from Shenzhen, China, and New York City, USA (the data have not been peer-reviewed). Among 383 patients from Shenzhen with COVID-19, overweight was associated with an 86% higher, and obesity with a 142% higher, risk of developing severe pneumonia compared with patients

of normal weight in statistical models that controlled for potential confounders<sup>6</sup>. Among 4,103 patients with COVID-19 at an academic health system in New York City, BMI  $>40$  kg/m<sup>2</sup> was the second strongest independent predictor of hospitalization, after old age<sup>7</sup>. Furthermore, in a small study from a university hospital in Lille, France, reporting data from 124 patients with COVID-19, the need for invasive mechanical ventilation was associated with a BMI  $\geq 35$  kg/m<sup>2</sup>, independently of other comorbidities<sup>8</sup>. The parameters mediating this high risk are thought to include impaired respiratory mechanics, increased airway resistance and impaired gas exchange, as well as other pathophysiological features of obesity, such as low respiratory muscle strength and lung volumes<sup>9</sup>.

## The obesity paradox

Conversely, an obesity survival paradox has been observed in patients with pneumonia. That is, despite the increased risk of pneumonia and difficulties of intubation and mask ventilation, the risk of death in patients with obesity and pneumonia might be decreased<sup>10</sup>. Potentially counter-balancing effects of obesity might include the more aggressive treatment provided to these patients, their increased metabolic reserve or other unidentified factors<sup>10</sup>. Thus, as a result of a potentially critical role of body weight or adiposity in determining the incidence and severity of pneumonia (and possibly other complications), it is important to collect anthropometric information for patients with COVID-19.

Furthermore, the impaired metabolic health (characterized by hypertension, dyslipidaemia and hyperglycaemia) associated with obesity might also be present in those with normal weight or overweight<sup>5</sup>. Prediabetes, which is present in 38% of the adult population in the USA, was identified as an important risk factor for CVD and renal disease<sup>5</sup>. To what extent these cardiometabolic risk factors predispose individuals to severe disease independently of BMI remains to be determined.

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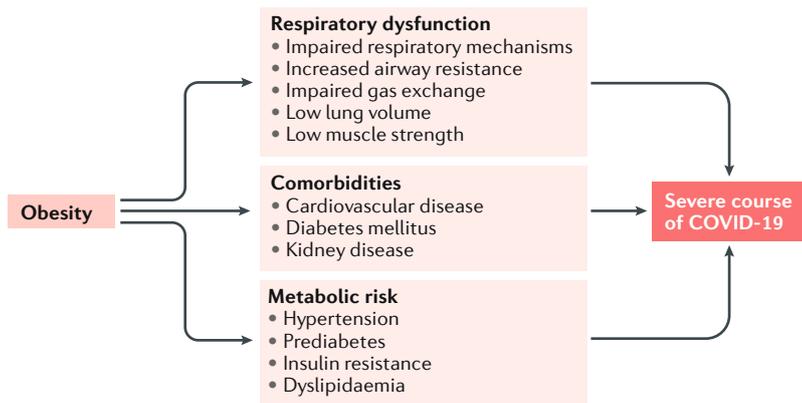
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**Fig. 1 | Obesity-related comorbidities and mechanisms of a severe course of COVID-19.** Patients with obesity often have respiratory dysfunction, which is characterized by alterations in respiratory mechanisms, increased airway resistance, impaired gas exchange and low lung volume and muscle strength. These individuals are predisposed to hypoventilation-associated pneumonia, pulmonary hypertension and cardiac stress. Obesity is also associated with an increased risk of diabetes mellitus, cardiovascular disease and kidney disease, comorbidities that are considered to result in increased vulnerability to pneumonia-associated organ failures. However, even in the absence of comorbidities of obesity, the presence of hypertension, dyslipidaemia, prediabetes and insulin resistance might predispose individuals to cardiovascular events and increased susceptibility to infection via atherosclerosis, cardiac dysfunction and impaired immune response.

### Conclusions

In conclusion, to better estimate the risk of complications in patients with COVID-19, in addition to evaluation of standard hospital parameters (such as the Sequential Organ Failure Assessment, d-dimer and pro-inflammatory markers), the measurement of anthropometric and metabolic parameters is crucial. These parameters include BMI, waist and hip circumferences and levels of glucose and insulin. The latter two parameters can be used for the estimation of insulin resistance, for example by calculation of the HOMA-IR. Knowledge about insulin resistance is important, because it is among the strongest determinants of impaired metabolic health, cardiac dysfunction and CVD-related mortality<sup>5</sup>.

Such measurements might be useful both in a primary care setting and in a hospital setting to assess the risk of a complicated course of disease in patients with a positive SARS-CoV-2 test (FIG. 1).

In conclusion, while it is widely recognized that the presence of comorbidities such as hypertension, diabetes mellitus and CVD is associated with a more severe course of COVID-19, obesity has hardly been investigated so far. Obesity is a main risk factor for these comorbidities and more generally for impaired metabolic health (such as dyslipidaemia and insulin resistance) and is also linked to an increased risk of pneumonia. Measurement of anthropometric characteristics and metabolic parameters is crucial to better estimate the risk of complications in patients with COVID-19.

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### Competing interests

D.S.L. has received royalties for books on nutrition and obesity. The other authors declare no competing interests.