Body mass index and acute respiratory distress severity in patients with and without SARS-CoV-2 infection

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Editor—In December 2019 a cluster of pneumonia cases of unknown aetiology was identified in Wuhan, China. A novel coronavirus was isolated from lower respiratory tract samples and identified as a specific severe acute respiratory syndrome coronovirus-2 (SARS-CoV-2).[1] An increasing number of patients around the world developed coronavirus disease 2019 (COVID-19), which primarily injures the vascular endothelium, with some developing acute respiratory distress (C-ARDS). C-ARDS is characterised by active lung inflammation and increases in lung vascular permeability and lung weight, as identified in the postmortem analysis of lung tissue from COVID-19 patients where features of the exudative and proliferative phases of diffuse alveolar disease were seen. However, COVID-19 is also associated with damage to the heart, CNS, kidneys, immune cells, and endothelial cells of arteries and veins. It has been reported that, among hospitalised patients with COVID-19, 60–70% presented with C-ARDS, and up to 30% required ICU admission with an associated mortality ranging from 26% to 78%.[2,3]

A recent report of 24 patients with COVID-19 showed that the average BMI was 33 kg m^{-2}.[4] Increased BMI is associated with an increased risk of developing ARDS with a similar risk of mortality.[5,6] Because of the high frequency of obesity reported among patients admitted in the ICU for C-ARDS,[7] we aimed to investigate if mechanically ventilated C-ARDS patients had a higher BMI compared with an historical group of consecutive ARDS patients requiring mechanical ventilation.

We conducted a retrospective analysis of 140 consecutive C-ARDS patients admitted to the ICU of San Paolo Hospital (Milan, Italy) and of Maggiore Hospital (Lodi, Italy) from February 25, 2020 to April 19, 2020. All patients had laboratory-confirmed SARS-CoV-2 infection diagnosis by RT–PCR of nasopharyngeal swabs. We compared C-ARDS patients with 247 consecutive 'other ARDS' patients enrolled in previous and ongoing studies (NCT03920189).[8] The Institutional Ethics Board of ASST Santi Paolo e Carlo, San Paolo University Hospital, Milan, Italy approved the study, and the Institutional Ethics Board of Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy approved this study for Maggiore Hospital, Lodi, Italy. The datasets used, analysed, or both during the current study are available from the corresponding author upon reasonable request.

Table 1 Baseline characteristics of study population. Quantitative data are expressed as mean (standard deviation, SD) or median (inter-quartile range) as appropriate. Categorical data are presented as *n* (%). Student's *t*-test or Wilcoxon–Mann–Whitney *U*-test, as appropriate, were used for continuous variable analysis, whereas χ^2 test was used for categorical variable analysis. Statistical analysis was performed with Stata 16 (StataCorp. Statistical Software: Release 16.0. Stata Corporation, College Station, TX, USA). *$P<0.05$. ARDS, acute respiratory distress; BMI, body mass index; SAPS II, Simplified Acute Physiology Score II.

Baseline characteristics	C-ARDS (*n*=140)	'Other ARDS' (*n*=247)	P
Age, yr	61 (10)	60 (16)	0.22
Male sex	84 (118)	68 (167)	<0.0001
Weight, kg	80 (75–90)	74 (61–85)	<0.0001
BMI, kg m^{-2}	28 (25–31)	25 (22–29)	<0.0001
BMI subclasses			
Underweight (BMI <18.5)	0 (0)	6 (14)*	<0.001
Healthy weight (BMI 18.5–24.9)	22 (30)	45 (111)*	
Overweight (BMI 25–29.9)	49 (69)	33 (82)*	
Obese class I (BMI 30–34.9)	18 (25)	8 (20)*	
Obese class II (BMI 35–39.9)	9 (13)	3 (9)	
Obese class III (BMI ≥40)	2 (3)	5 (11)	
SAPS II	33 (28–41)	41 (32–54)	<0.0001
PEEP, cm H_2O	12 (10–14)	10 (10–12)	<0.0001
PaO_2/FiO_2 ratio, mm Hg	120 (90–165)	169 (127–216)	<0.0001
ARDS severity			<0.0001
Mild	14 (19)	31 (78)*	
Moderate	50 (70)	56 (138)	
Severe	36 (51)	13 (31)*	

BMI was significantly higher in C-ARDS compared with 'other ARDS' patients (28 [25–31] *vs* 25 [22–29] kg m^{-2}, $P<0.0001$). Characteristics of the study populations are shown in Table 1. We found a significantly higher percentage of overweight (BMI 25–29.9 kg m^{-2}) and obese (BMI ≥30 kg m^{-2})

patients in C-ARDS than in 'other ARDS' population admitted in ICU (49% *vs* 33% and 29% *vs* 16%, respectively; $P<0.0001$). Similar findings have been reported for hospitalised patients with 2009 pandemic H1N1 infection: 32.5% were obese and 22.5% were morbidly obese.[9]

At the time of ICU admission, mechanically ventilated C-ARDS patients had a ratio of arterial oxygen partial pressure to fractional inspired oxygen (PaO_2/FiO_2) significantly lower (120 [90–165] *vs* 169 [127–216] mm Hg, $P<0.0001$) with PEEP significantly higher (12 [10–14] *vs* 10 [10–12] cm H_2O, $P<0.0001$). According to the Berlin ARDS definition, we found that the percentage of severe ARDS patients was significantly higher in C-ARDS patients (36% *vs* 13%, $P<0.0001$).

We also calculated the adjusted odds ratios (OR) and 95% confidence intervals (CI) from a multivariable logistic regression model containing the covariates sex (male *vs* female), age (<50 yr, 5 yr groups from 50 to 74 yr, and >75 yr), and BMI subclasses (reference healthy weight). We found adjusted ORs of 2.15 (95% CI, 1.20–3.84) for males, 3.27 (1.88–5.69) for overweight, and 3.42 (1.79–6.52) for obese patients.

The well-known characteristics of obese ARDS patients, including an increase in chest wall elastance, reduction in functional residual capacity, and possible impairment of inspiratory muscles, can be associated with a higher risk of atelectasis formation, failure of noninvasive ventilatory support, and need for invasive mechanical ventilation. We speculate that the presence of more adipose tissue, with an associated higher number of angiotensin-converting enzyme 2 (ACE2) receptors, favours penetration of the virus and increases vulnerability to infection, as ACE2 receptors are used by SARS-CoV-2 to enter cells.[10] ACE2 receptors have a wide distribution in several tissue types; in the pancreas, SARS-CoV-2 induces hyperglycaemia even in non-diabetic individuals,[11] which in turn aggravates the cytokine storm.[12]

We found that, among patients admitted to the ICU and requiring mechanical ventilation, the group of patients with C-ARDS included a higher percentage of patients with BMI ≥ 25 kg m^{-2} and a higher percentage of patients with severe ARDS compared with those who have 'other ARDS'. We also found strong associations between C-ARDS and male sex and with overweight/obese patients. Our results suggest that a possible relationship between higher BMI and development of severe ARDS could exist among C-ARDS patients. Our data are not adjusted for background factors in the C-ARDS and ARDS groups, including information about chronic diseases. A larger population including patients admitted and not admitted to ICU is necessary to determine if BMI is a risk factor for C-ARDS and for development of severe ARDS.

Declarations of interest

The authors declare that they have no conflicts of interest.

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