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Nutritional risk, not obesity, is associated with mortality in critically ill COVID-19 patients

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ABSTRACT

Background: Despite the identification of obesity as a risk factor for higher rates of hospital and Intensive Care Unit (ICU) admissions and complications due to COVID-19, the association between obesity and mortality in critically ill COVID-19 patients remains controversial, and the nutritional risk is little considered. Hence, our study sought to evaluate the association between obesity, nutritional risk, and mortality in critically ill patients diagnosed with COVID-19.

Methods: Retrospective study were condutcted including adult critically ill COVID-19 patients admitted to an ICU between April 2020 and March 2021. Clinical and laboratory data were collected from electronic medical records. Obesity was classified by body mass index ≥ 30 kg/m^2. A mNUTRIC score of ≥ 5 indicated high nutritional risk. Multiple Cox Regression was used to estimate the association between mNUTRIC, obesity, and mortality.

Results: From 71 patients aged 59 ($\pm$ 15) years, 71.8 % were male. The frequencies of obesity (58.7 %) and death (49.3 %) were high, but obesity was not associated with mortality. Based on mNUTRIC, 85.9 % of patients were at high nutritional risk, presenting a higher frequency of mortality than patients at low nutritional risk (50.8 % vs 40.0 %; $p = 0.014$). Multiple Cox Regression showed that for each unit increase in mNUTRIC score the probability of death almost doubled, regardless of the presence of obesity (HR = 1.74; $p < 0.001$).

Conclusions: A higher nutritional risk was positively associated with mortality in critically ill COVID-19 patients, regardless of obesity, showing the importance of early identification of nutritional risk for appropriate nutritional interventions in this population.

1. Introduction

In March 2020, the World Health Organization (WHO) declared a global pandemic caused by the SARS-CoV-2 virus. Since then, COVID-19 has evolved with wide geographical impact, affecting much of the world's population. Several risk factors have been associated with greater severity of the disease, such as older age and male gender, and some chronic diseases like diabetes, hypertension, and cardiovascular diseases [1], with obesity representing a risk factor for greater COVID-19 complications. [2,3].

Obesity has been identified as an important risk factor for hospital admissions, need for mechanical ventilation, Intensive Care Unit (ICU) admission, and critical condition in COVID-19 patients [4–7]. However, the association between obesity and mortality in critically ill patients remains poorly described, with studies showing conflicting results [8–10]. While some studies found no effect of obesity on mortality [11,

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12], others showed that a higher body mass index (BMI) had protective effects [13]. A third group of studies found higher mortality among patients with obesity [14,15].

Besides, the nutritional risk is little considered in such studies. Impaired nutritional status has already been associated with higher inflammatory response, compromised immune functions, and increased risk of infection [16,17]. Considering the high frequency of patients with nutritional risk at admission [18], the nutritional deficits may be factors associated with hospital mortality, convalescence, and higher hospital costs [19]. As recommended by expert consensus, nutritional risk should be identified early in hospitalized patients [20]. In the ICU setting, the identification of nutritional risk aims to evaluate patients at risk of developing worse outcomes when an earlier or more aggressive nutritional support is not prescribed. The NUTrition Risk in the Critically Ill (NUTRIC score) was the first nutritional risk assessment tool developed and validated specifically for critically ill patients [21], and in its original article it was demonstrated that nutritional adequacy modifies the association between this score and mortality. Although mNUTRIC is a good predictive factor associated with worse prognosis, including mortality in COVID-19 patients [22], obesity was not considered in these analyzes.

To our knowledge, the association between nutritional risk and mortality in critically ill COVID-19 patients with obesity has not yet been investigated. In this scenario, our study sought to evaluate the association between obesity, nutritional risk, and mortality in critically ill patients diagnosed with COVID-19, admitted to an ICU.

2. Material and methods

2.1. Study design and population

This retrospective documentary study was carried out between April 2020 and March 2021 in the Intensive Care Unit of the Hospital das Clínicas of Ribeirão Preto Medical School - University of São Paulo (HCFMRP-USP), in Ribeirão Preto, São Paulo, Brazil, which is a public tertiary level hospital reference on COVID-19 treatment. This ICU was dedicated exclusively to the care of COVID-19 patients. This study was approved by the Research Ethics Committee of the HCFMRP-USP, approval no. 4.403.078.

The inclusion criteria were: adult patients (age $\geq$ 18 years old) of both genders who were admitted to the ICU in the period of the study with COVID-19 diagnosis. All patients admitted in the ICU were considered as COVID-19 critically ill patients following the WHO definition [23]. No patients were excluded, so all adult and older patients admitted to the ICU of the aforesaid hospital in the period were included in the analysis, totaling 71 patients.

2.2. Data collection

Demographic data (gender and age), clinical diagnoses, length of hospital stay, vital signs, clinical data (ventilatory devices, use of vasoactive medication, need for renal replacement therapy, and prone position), medication use, nutritional information (weight, height, prescribed nutritional therapy), and laboratory tests (CBC, albumin, C-reactive protein, lactate, and blood glucose) were collected from the patient's electronic medical records. All the data were collected from the patient's electronic medical records through a data extraction system. If there was any important information observed just in the paper forms, after the extraction, the data were collected manually by the authors from each patient's electronic medical records.

Data from the first 24 h of each patient's ICU admission were considered for vital signs, tests, ventilatory modes, nutritional therapy, and vasoactive drugs. In each patient's electronic medical records there was information on the exact time of admission in the ICU by the hospital system and the data collected referred to the 24 h hours following this admission.

Ventilatory devices were categorized as oxygen therapy (nasal oxygen catheter, reservoir mask, Venturi mask, and high-flow catheter), noninvasive mechanical ventilation (NIMV; bilevel positive airway pressure – BIPAP, continuous positive airway pressure – CPAP), and invasive mechanical ventilation (IMV; patients on mechanical ventilation, intubated or tracheostomized).

As for treatments and medications, renal replacement therapy and prone position were categorized as yes/no throughout hospitalization, except vasoactive drugs, which were considered in the first 24 h of ICU stay.

Acute Physiology and Chronic Health Evaluation II (APACHE II) [24], and the Sequential Organ Failure Assessment (SOFA) [25] were calculated using clinical and laboratory information collected within the first 24 h of ICU admission.

2.3. Obesity

Body mass index was calculated by dividing body weight (kg) by the square of height (m), classifying the patients as with obesity (BMI $\geq$ 30 kg/m^2) and without obesity (BMI $<$ 30 kg/m^2) [26].

2.4. Nutritional risk classification

Nutritional risk was assessed by the modified NUTRIC score (mNUTRIC), which consists of the NUTRIC score minus the interleukin-6 values, thus comprising five variables: age, number of comorbidities, days from hospital admission to ICU admission, APACHE II score, and SOFA score. Patients with mNUTRIC scores $\leq$ 4 at their ICU admission were considered as low nutritional risk, and $\geq$ 5 scores as high nutritional risk [21].

2.5. Sample observation power

As all patients diagnosed with COVID-19 admitted to this ICU during the evaluated period were included in the sample, all available data were used. Post hoc analysis was performed by means of Poisson's Regression (closest to Cox Regression and considered for frequent outcomes), alpha of 0.05, $\beta 1$ of 1.74, and a sample size of 71 using G*Power software (V.3.1.9.6). Observation power was estimated at 0.99, which means the sample was sufficient for the analysis.

2.6. Statistical analysis

The Kolmogorov-Smirnov was used as a variable distribution test. Symmetric variables in the bivariate analysis were presented as mean and standard deviation and analyzed by Student's t-test. Asymmetric variables were presented as median and interquartile intervals and analyzed by the Mann-Whitney test. Categorical variables were expressed as proportions and analyzed by the Chi-square or Fisher's exact tests. The association between mNUTRIC score (main exposure), obesity (BMI $\geq$ 30 kg/m^2) according to the length of hospital stay (days) until the death event (yes – 1 /no – 0) was estimated by Multiple Cox Regression. Since the mNUTRIC score includes information on age, comorbidities, APACHE II, and SOFA values (calculated considering clinical and laboratory information), model adjustments were performed without these data to avoid multicollinearity. Cumulative survival curves adjusted were performed to show the results with or without obesity, and low or high nutritional risk. All analyzes were carried out using the Statistical Package for the Social Science software (SPSS v.25) and differences were considered statistically significant when $p < 0.05$.

3. Results

3.1. Population characteristics

Of the 71 critically ill COVID-19 patients included in this study that represented all patients admitted in the period (Table 1), the mean age was 59 ± 15 years, 71.8 % (n = 51) were male, and 67.6 % (n = 48) had two or more comorbidities. The median length of ICU stay was 12 days (6–22 days), and the total length of stay was 22 days (13–36 days).

On the first day of ICU admission, 55 patients (77.5 %) were placed on invasive mechanical ventilation, and 54 (76 %) received vasoactive drugs. During hospitalization, 29 patients (40.8 %) underwent hemodialysis and 44 patients (62 %) were placed in prone position at least once. In the first 24 h in the ICU, 46 individuals (64.8 %) received enteral nutritional therapy, 24 (33,8 %) were prescribed fasting and one individual (1,4 %) were placed on oral diet.

3.2. Obesity

Of the 71 patients, 41 (57.7 %) had obesity and a frequency of two or more comorbidities (82.9 %). The median length of ICU stay among patients with obesity was 19 days and 13 days for patients without obesity (p = 0.424). Regarding the hospital length of stay, patients with obesity showed a median of 20 days and those without obesity had a median of 26 days (p = 0.377). During hospitalization, most patients with obesity were placed in prone position (p = 0.034). We found no statistically significant difference regarding the other therapies and mortality rates. On the first day of ICU admission, patients with obesity showed higher albumin (p = 0.02) and $PaCO_2$ (p = 0.018) values, and lower PaO_2 (p = 0.010) (Table 1).

3.3. Nutritional risk

Patients classified as high nutritional risk (89.5 %) had higher percentages of invasive mechanical ventilation (p < 0.001), vasoactive drugs use (p < 0.001), and kidney injury during hospitalization (p = 0.033). When compared with patients at low nutritional risk, patients at high nutritional risk had higher FiO_2 (p = 0.015) and creatinine (p = 0.011) values in the first 24 h in the ICU (Table 1).

3.4. Mortality

The frequency of mortality was 49.3 %, with higher occurrence among the high nutritional risk group (50.8 % vs 40.0 %; p = 0.014). Deceased patients were significantly older, with a higher number of comorbidities and higher APACHE and SOFA values. Non-survivors showed a higher frequency of acute kidney injury (p < 0.001), renal replacement therapy (p < 0.001), and prone position (p = 0.035) during hospitalization. They also had a higher frequency of invasive mechanical ventilation (p = 0.048) and need for vasoactive drugs (p < 0.001) in the first 24 h in the ICU, besides lower albumin levels (p = 0.038) (Table 1).

Higher nutritional risk increased the probability of death almost twofold (OR = 1.74 for each unit increase in mNUTRIC score; p < 0.001), regardless of the presence of obesity (Table 1). Fig. 1 shows that the cumulative survival is similar between patients with and without obesity and different when we evaluate the nutritional risk, thus reinforcing the previous results. Obesity was not associated with higher mortality (p = 0.980) (Table 2, Fig. 1).

4. Discussion

Our study showed that obesity alone was not a predictor of mortality in critically ill patients. Nutritional risk was highly prevalent (85.9 %), with each unit increase in mNUTRIC increasing the risk of death almost twofold. To our knowledge, this was the first study to analyze the association between nutritional risk and mortality in critically ill COVID-19 patients with and without obesity.

We found a hospital mortality frequency of 49.3 %. Oscillations in mortality can occur during time, COVID-19 waves/variants and progress of vaccination programs. The percentage of mortality found in this study was higher than found in a multicentre cohort study (31.7 % of ICU mortality in the first COVID-19 wave and 28.8 % in the second/third waves) [27]. Considering that the Brazilian vaccination campaign started in January, 2021, it's likely that a small percentage of patients were fully vaccinated in this study.

Lower frequencies of high nutritional risk have been reported in critically ill COVID-19 patients. Zhang et al. and Padilla et al. noted that 61 % and 66 % of the patients showed high nutritional risk, respectively [22,28]. Zhang et al also showed that patients with mNUTRIC score ≥ 5 had higher mortality and probability of ICU death over 28 days (OR: 2.01, p = 0.006). Neither study, however, explored obesity in their analysis. Zhang et al also showed that patients with high nutritional risk identified by mNUTRIC had higher mortality and probability of ICU death over 28 days (OR: 2.01, p = 0.006). Li et al. [29] showed that NUTRIC independently predicted the risk of hospital death (OR: 1.19, p = 0.006) and the length of stay, but not considering obesity again. Additionally, Martinuzzi et al. [30] demonstrated that non-survivors had higher comorbidities frequencies and higher nutritional score values (NRS, 2002) [57] even when adjusted by obesity, as observed in our sample.

Nutritional risk is a commonly neglected condition, especially in patients with obesity. Studies indicate that about one-third of hospitalized patients with obesity are at nutritional risk [31,32]. In the present study this percentage was even higher (60.7 %). Since the most nutritional risk screening tools use anthropometric indicators such as low BMI and weight loss percentage, the frequency of nutritional risk may be underestimated in patients with obesity. The NUTRIC score, on the other hand, does not use anthropometric data and thus seems a suitable tool for the nutritional assessment of critically ill patients with obesity. Its applicability, however, has not yet been well investigated in this population.

Our analysis found an overall frequency of obesity of 57.7 %, higher than the frequencies of 49 % and 41.7 % shown by previous Chinese and American studies, respectively [33,34]. Moreover, obesity had no effect on in-hospital mortality, similar to a recent meta-analysis with COVID-19 and pneumonia patients [35]. This study, however, did not include research on nutritional risk. In the subset of critically ill patients without COVID-19, some studies reported on an "obesity paradox" – an inverse association between obesity and mortality [36,37]. Dana et al. [13] observed this same paradox in critically ill COVID-19 patients but neglected to consider nutritional risk.

The present study found no association between obesity and mortality. Jagan et al. [38] noted that the protective effect of higher BMIs on mortality may not occur when considering disease severity, quantified as hypotension, higher lactate, and increased APACHE score. All the patients analyzed here presented these severity characteristics, showing lactate means above the reference values and high APACHE score values.

BMI is a commonly used index to assess obesity and studies indicate that body composition may be associated with adverse outcomes. In COVID-19 hospitalized patients with obesity, the higher visceral and intermuscular adipose tissue and muscle mass losses can be predictors of mortality [39]. Besides that, the muscle mass depletion could determine poor prognosis and mortality in hospitalized and critically ill patients [40–42]. However, the alterations in body composition during the hospital stay could make the nutritional risk higher, contributing to mortality beyond obesity per se.

In this study, individuals with obesity showed worse ventilatory parameters: higher prevalence of IMV, higher FiO_2 , and lower PaO_2 values. Retrospective studies and meta-analyses have identified obesity as a risk factor for respiratory diseases and found higher percentages of patients with obesity requiring mechanical ventilation [35]. Central

Table 1
Demographic and clinical characteristics of the study population.

Variables	Total	Without obesity	Obesity	P-value	Nutritional risk		P-value	Survivors	Non-survivors	P-value
	(n = 71)	(n = 29, 40.8 %)	(n = 41, 57.7 %)		Low (n = 10, 14.1 %)	High (n = 61, 85.9 %)		(n = 36, 50.7 %)	(n = 35, 49.3 %)	
	Mean ± SD Median (P25–P75) n (%)									
Baseline characteristics										
Age (years)	59.56 ± 14.94	58.9 ± 17.13	59.73 ± 13.46	0.820	48.40 ± 16.08	63.94 ± 12.04	0.019†	54.14 ± 16.16	65.14 ± 11.31	0.001†
Gender, Male	51 (71.80)	23 (79.30)	27 (65.90)	0.220†	8 (80)	43 (70.50)	0.536	29 (80.55)	22 (62.65)	0.097
Number of comorbidities										
0–1	23 (32.40)	15 (51.70)	7 (17.10)	0.002	7 (70)	16 (26.20)	0.006	15 (42.90)	7 (19.50)	0.028
≥ 2	48 (67.60)	14 (48.30)	34 (82.90)		3 (30)	45 (73.80)		20 (57.10)	29 (80.50)	
APACHE II	27.42 ± 6.57	26.83 ± 7	28.17 ± 5.97	0.391†	20.80 ± 6.14	30 ± 4.70	< 0.001†	24.06 ± 6.27	30.86 ± 4.97	< 0.001†
SOFA	12 (10–14)	11 (9–14)	12 (11–13.50)	0.250*	7.5 (1.75–9)	12 (11–14)	< 0.001*	11 (9–12)	13 (12–15)	< 0.001*
mNUTRIC	7 (5–8)	7 (5–7)	7 (6–8)	0.119*	3.5 (1.75–4)	7 (6–8)	< 0.001*	6 (4.25–7)	8 (7–8)	0.008*
BMI (kg/m^2)										
< 18.5	1 (1.40)	1	0	–	0	1 (1.60)	0.420	1 (2.77)	0	0.340
18.5–24.9	12 (17.10)	12 (41.40)	0		1 (11.10)	11 (18)		4 (11.11)	8 (22.22)	
25–29.9	16 (22.90)	16 (55.20)	0		4 (44.40)	12 (19.70)		10 (27.78)	6 (16.67)	
≥ 30	41 (58.60)	0	41 (100)		4 (44.40)	37 (60.70)		20 (55.55)	21 (58.33)	
AKI	43 (60.60)	18 (62.10)	25 (61)	0.926	3 (30)	40 (65.60)	0.033	15 (41.67)	28 (77.78)	< 0.001
Ventilatory modes										
Spontaneous ventilation	1 (1.40)	1 (3.40)	0	0.316	0	1 (1.60)	0.001	1 (2.77)	0	0.048
Oxygen therapy	4 (5.60)	2 (6.90)	2 (4.90)		3 (30)	1 (1.60)		3 (8.33)	1 (2.85)	
NIV	11 (15.50)	2 (6.90)	8 (19.50)		3 (30)	8 (13.10)		9 (25)	2 (5.71)	
MV	55 (77.50)	24 (82.80)	31 (75.60)		4 (40)	51 (83.60)		23 (63.89)	32 (91.42)	
FiO_2 (mmHg)	100 (80–100)	100 (65–100)	100 (100–100)	0.203*	45 (7.75–100)	100 (100–100)	0.015*	100 (50–100)	100 (100–100)	0.002*
Nutritional therapy										
Enteral	46 (64.80)	20 (69)	26 (63.40)	0.630	4 (40)	42 (68.90)	0.077	23 (63.90)	23 (65.71)	0.872
Oral	1 (1.4)	0	1 (2.4)	0.397	1 (10)	0	0.013	1 (2.77)	0	0.321
Laboratory tests										
Albumin (g/dL)	3.3 (3–3.60)	3.2 (2.77–3.32)	3.4 (3.10–3.70)	0.020*	3.40 (3.22–3.82)	3.30 (3–3.55)	0.301*	3.40 (3.30–3.75)	3.20 (2.85–3.45)	0.038*
Cr (mg/dL)	1.5 (1.07–2.84)	1.27 (1.06–2.20)	1.66 (1.06–3.41)	0.194*	0.97 (0.86–1.28)	1.61 (1.19–3)	0.011*	1.30 (1.02–1.97)	1.69 (1.07–3.40)	0.088*
RB (million/mm^3)	4.20 ± 0.86	3.97 ± 1	4.36 ± 0.72	0.063†	4.41 ± 0.87	4.17 ± 0.86	0.432†	4.27 ± 0.96	4.14 ± 0.76	0.590†
Hb(g/dL)	12.50 ± 2.60	11.89 ± 2.90	12.91 ± 2.28	0.103†	13.05 ± 1.64	12.40 ± 2.70	0.489†	12.60 ± 2.78	12.40 ± 2.43	0.784†
Hematocrit (%)	37.48 ± 7.70	36 ± 8.70	39.14 ± 6.76	0.092†	39.44 ± 5.34	37.06 ± 7.97	0.507†	38.02 ± 8.07	37.65 ± 7.38	0.625†
White blood cells (× 10 * 9/L)	11.45 (7.75–14.10)	10.30 (6.75–12.80)	11.8 (8.80–14.80)	0.198*	7.90 (6.30–11.80)	11.80 (8.70–14.15)	0.105*	10.60 (7.30–14.10)	11.70 (8.10–14.20)	0.565*
Platelets (×10 * 9/L)	221.50 (160.50–274.25)	200 (133.5–240)	251 (192.50–299)	0.005*	211 (153–235.50)	233 (150–283)	0.888*	236 (180–290)	208 (149–268)	0.194*
CRP (mg/dL)	16.27 ± 10.57	15.29 ± 9.69	17.17 ± 11.46	0.533†	17.80 ± 11.92	15.75 ± 10.39	0.639†	16.12 ± 10.94	16.44 ± 10.32	0.915†
Lactate (mmol/L)	2.73 ± 1.84	2.84 ± 1.79	2.40 ± 0.78	0.163†	3.43 ± 3.69	2.62 ± 1.34	0.203†	2.94 ± 2.43	2.52 ± 0.90	0.986†
Blood glucose (mg/dL)	157.50 (130.50–286.75)	149 (103–281)	157.5 (143–304.75)	0.398*	117 (88–217.25)	178 (143–301)	0.098*	148.5 (124–216.75)	237 (133–319)	0.235*
Arterial blood gas										
PaO2 (mmHg)	76.2 (62.20–90.50)	82.50 (72.60–97.95)	68.2 (55.65–83.50)	0.010*	71.4 (58.32–100.55)	78 (61.70–91.75)	0.823*	75.40 (56.80–84)	81.4 (63.40–93)	0.411*
PaCO2 (mmHg)	42.9 (37.20–49.30)	40.8 (34.75–47.55)	43.8 (39.60–56.05)	0.029*	37.8 (32.65–42.95)	43.70 (38.40–52.95)	0.140*	41.60 (35.72–48.77)	45.30 (39.50–50.20)	0.202*
Treatments/medications (yes/no)										
VAD	54 (76)	20 (69)	34 (82.90)	0.171	3 (30)	52 (85.20)	< 0.001	21 (58.22)	34 (97.14)	< 0.001
Overall clinical outcomes										
RRT	29 (40.80)	11 (37.90)	17 (41.50)	0.766	2 (20)	27 (44.30)	0.148	7 (19.44)	22 (62.85)	< 0.001
Prone position	44 (62)	14 (48.30)	30 (73.2)	0.034	4 (40)	40 (65.60)	0.123	18 (50)	26 (74.28)	0.035
ICU LoS (days)	12 (6–22)	10 (4–21.50)	13 (8–22.50)	0.424*	7.5 (4–17.75)	13 (6.50–22)	0.701*	10 (5–17)	15 (8–25)	0.152*
Hospital LoS (days)	22 (13–36)	26 (16.5–38)	20 (12.5–36)	0.377*	18 (9–38.25)	23 (15–36)	0.181*	23 (16–40.50)	22 (11–33)	0.210*
Death	35	14 (48.30)	21 (51.20)	0.808	4 (40.0)	31 (50.80)	0.014	–	–	–

Abbreviations: APACHE II, Acute Physiology and Chronic Health Evaluation II; AKI, acute kidney injury; BMI, body mass index; FiO2, fraction of inspired oxygen; Cr, Creatinine RB, Red blood cells; Hb, Hemoglobin; mNUTRIC, modified *NUTrition Risk in the Critically Ill*; MV, mechanical ventilation; NIV, non invasive ventilation; Red blood cells PaCO2, partial pressure of carbon dioxide; PaO2, partial pressure of oxygen; CRP, C-reactive protein; RRT, renal replacement therapy; SOFA, Sequential Organ Failure Assessment; VAD, vasoactive drugs. LoS, length of stay.

* Mann-Whitney test.

† Student's T test.

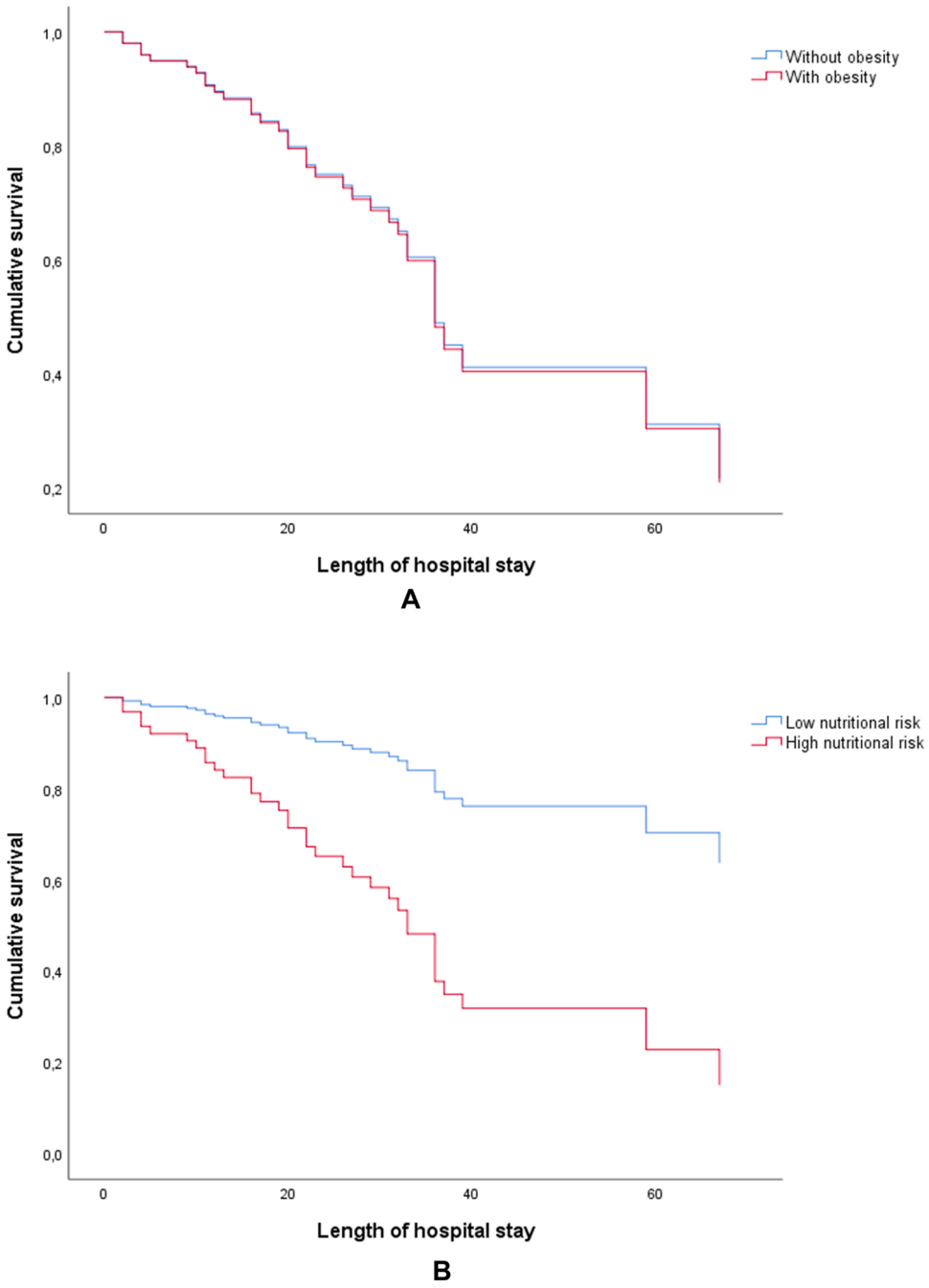

Fig. 1. A: Cumulative survival curves of patients with and without obesity by length of hospital stay (days), adjusted by mNUTRIC score. **B**: Cumulative survival curves of patients with low and high nutritional risk adjusted by BMI (kg/m^2).

Table 2
Multiple Cox Regression to estimate the association of nutritional risk (mNUTRIC) and obesity with hospital mortality.

Variables	Hazard ratio (95 % CI)	P-value
mNUTRIC score	1.74 (1.32–2.29)	< 0.001
Obesity (BMI ≥ 30 kg/m^2)	0.98 (0.48–1.99)	0.955

BMI. body mass index; CI. confidence interval; mNUTRIC. modified *NUTrition Risk in the Critically Ill*.

obesity is associated with poor ventilation at the base of the lung, resulting in reduced oxygen saturation [43] and increased airway resistance [44], which could contribute to those findings. Other studies have observed that obesity is an independent risk factor for intubation [45] and that the anatomical characteristics of these individuals seem to contribute to greater difficulties in ventilation.

Several factors are associated with hospital mortality of critically ill COVID-19 patients. Our study found a high prevalence of comorbidities (67.6 % of patients with two or more), significantly more frequent among patients with obesity, at high nutritional risk, and among the deceased. Although the association between comorbidities and higher mortality in COVID-19 patients is well documented [46–48], its mechanisms are still unknown. In diabetes mellitus and systemic arterial hypertension, patients taking antihypertensive ACE-2 inhibitors and angiotensin receptor blockers can show increase ACE-2 expression on the cell surface [49]. A similar situation has been documented in patients with diabetes [50], which may promote greater virus absorption and infection. Also, the prolonged low-grade inflammation promotes a

pro-inflammatory state with changes in the immune system and endothelial dysfunction, thus contributing to greater severity of COVID-19 [51–53].

The NUTRIC score is an important tool to identify patients who may benefit most from more aggressive nutritional therapy [21]. In our analysis, on the first day of ICU admission, about 65 % of patients were prescribed enteral nutrition, 1 % were placed on oral diet, and 34 % of patients were prescribed fasting. In a Chinese study [29], it was noted that 37.9 % of the patients started nutrition therapy after > 48 h and in a Latin American study, patients presented a medium time of 2.6 days to initiate nutrition support [30]. International consensus recommends early nutritional treatment for critically ill COVID-19 patients. The European Society of Clinical Nutrition and Metabolism (ESPEN), for example, advises that treatment begins within 24–48 h of hospital admission. Early enteral nutrition can lead to fewer infectious complications and shorter ICU stay [54–56]. Some clinical conditions such as shock and progressive doses of vasoactive drugs, however, may delay the initiation of nutritional support. In the present study, 76 % of patients received some vasoactive drug on the first day of ICU admission, which could have contributed to the high frequencies of fasting.

The present study showed that obesity alone was not a predictor of mortality and that a higher mNUTRIC score was associated with mortality. Critically ill COVID-19 patients presented high frequencies of obesity, mortality, and high mNUTRIC score values. Our study has limitations inherent to single-center retrospective studies. Nine patients had no bilirubin results in the first 24 h in the ICU. We thus assumed normal bilirubin values for these patients to perform the SOFA calculation, inferring a more conservative estimate, which may have underestimated the disease severity and the mNUTRIC score.

5. Conclusion

Critically ill COVID-19 patients had high nutritional risk (85.9 %), obesity (57.7 %), and mortality (49.3 %). The risk of death was positively associated with high nutritional risk, regardless of the presence of obesity. Early identification of nutritional risk is of paramount importance for appropriate nutritional interventions in this population. Despite the lack of a gold standard for identifying nutritional risk in critically ill patients with COVID-19, the mNUTRIC can be an appropriate tool for this purpose. Additional studies are also needed to analyze the role of obesity in the mortality of COVID-19 patients.

CRediT authorship contribution statement

ACPS: Investigation, Writing – original draft, Writing – review & editing. **CCJ:** Conceptualization, Supervision, Writing – review & editing. **CRP:** Investigation, Resources. **TCPL:** Investigation, Resources. **WJL:** Investigation, Resources. **GGP:** Methodology, Formal analysis, Data curation, Writing – review & editing.

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Conflict of interest

The authors declare no conflict of interest.

Data statement

The data that support the findings of this study are available from the corresponding author, upon reasonable request.

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