Submitted: 16 December, 2023 Accepted: 02 February, 2024 Published: 08 July, 2024 DOI:10.22514/sv.2024.082

Open Access
Signa Vitae

ORIGINAL RESEARCH

# Protective effect of high body mass index in elderly critically ill with severe COVID-19 pneumonia

Marko Kurnik[1,†], Helena Božič[1,†], Anže Vindišar[1], Petra Kolar[1], Matej Podbregar[1,2,*]

[1]Department of internal intensive care, General Hospital Celje, 3000 Celje, Slovenia
[2]Faculty of Medicine, University of Ljubljana, 1000 Ljubljana, Slovenia

***Correspondence**
matej.podbregar@guest.arnes.si
(Matej Podbregar)

[†] These authors contributed equally.

## Abstract

The "obesity paradox"—reduced mortality in obese patients—in critically ill individuals remains a topic of conflicting evidence, but it appears to be more pronounced in the elderly. Our study aims to investigate the predictive significance of body weight in relation to the mortality of critically ill elderly individuals with severe COVID-19 pneumonia. Consecutive patients aged ≥70 years, admitted to intensive care unit (ICU) for SARS-CoV-2 severe pneumonia were included in the final analysis. Among various data collected, body mass index (BMI) was recorded upon admission, and both classical statistics and logistic regression modeling were applied to assess the relation of BMI with ICU mortality. Our cohort comprised 102 patients, with an average age of 77 ± 5 years, of whom 26% were female. The average length of ICU stay was 11.4 ± 9.2 days, and the average BMI was 29.3 ± 5.2 kg/m$^2$. High-flow oxygenation, non-invasive ventilation, and invasive mechanical ventilation were used to support 33%, 35%, and 68% of patients, respectively. ICU mortality was observed in 50.0% of cases, with survivors having a shorter ICU stay compared to non-survivors (9.1 ± 8.5 *vs.* 13.6 ± 9.4 days, $p = 0.01$). Furthermore, survivors exhibited higher BMI values compared to non-survivors (30.5 ± 5.6 *vs.* 28.1 ± 4.5 kg/m$^2$, $p = 0.02$), with a higher proportion of survivors having a BMI ≥30 kg/m$^2$ (51% *vs.* 29%, Chi-square $p = 0.025$). Adjusted for gender and chronic diseases, BMI ≥30 kg/m$^2$ measured at admission was associated with lower ICU mortality (odds ratio (OR): 0.33, $p = 0.04$) and lower hospital mortality (OR: 0.21, $p = 0.024$). Overall, our findings suggest that higher BMI is correlated with lower mortality and shorter ICU stays in elderly critically ill patients with severe COVID-19 pneumonia.

## Keywords

Body mass index; COVID-19; Critical care; Elderly; Intensive care unit; Mortality

## 1. Background

Obesity is characterized by an abnormal or excessive accumulation of fat that can adversely affect health. Nutritional status is classified using Body Mass Index (BMI), calculated as an individual's weight in kilograms divided by the square of their height in meters (kg/m$^2$). According to the World Health Organization (WHO), obesity in adults is defined as a BMI equal to or greater than 30 kg/m$^2$, while overweight is defined as a BMI equal to or greater than 25 kg/m$^2$ [1].

Obesity has been associated with an increased risk of developing Adult Respiratory Distress Syndrome (ARDS) and the need for invasive mechanical ventilation in COVID-19 patients [2]. Obese patients with COVID-19 face an elevated likelihood of requiring admission to the Intensive Care Unit (ICU) [2–6]. Several studies suggested a stronger impact of obesity in younger patients, identifying them as an especially high-risk group for worse outcomes [2, 7]. In individuals with obesity, viral infections often lead to a compromised immune response, triggering a "cytokine storm" characterized by the excessive production of pro-inflammatory cytokines. This cascade effect can lead to vascular hyperpermeability and multiorgan failure, resembling the severe manifestations observed in COVID-19 patients [2, 8].

However, the association between BMI and mortality has been conflicting, with some studies suggesting higher mortality in obese patients and others suggesting an inverse relationship, often termed the "obesity paradox" [2, 9, 10]. The obesity paradox is well known in heart failure and cancer patients [11]. It seems to be stronger in elderly [12]. Additionally, obesity has been associated with reduced mortality in patients with ARDS [13]. Several pathophysiological explanations for the obesity paradox exist, encompassing factors such as greater metabolic reserve in obese patients and variations in pulmonary mechanics and immunological aspects when comparing obese and non-obese individuals [3]. As of now, there is no evidence substantiating the existence of the obesity paradox in patients with COVID-19, whether they are younger or


  

elderly.

Since the obesity paradox seems to be stronger in elderly [12], our study was aimed to explore the relationship between BMI and mortality in elderly patients admitted to our ICU due to severe COVID-19 pneumonia. Our null hypothesis posited that there is no association between BMI and mortality within our patient cohort.

## 2. Methods

### 2.1 Setting

A retrospective cohort study was carried out in a combined 25-bed, level 3 ICU at General and Teaching Hospital Celje, Slovenia, spanning a 12-month period from March 2020 to February 2021.

### 2.2 Patients

This ICU was exclusively designated for the treatment of adult ($\geq$18 years old) SARS-CoV-2 positive patients. COVID-19 diagnosis was established through the identification of a positive result in at least one real-time polymerase chain reaction (RT-PCR) test for SARS-CoV-2, conducted on respiratory specimens such as nasopharyngeal swab, sputum or lower respiratory tract specimens. All consecutive patients aged 70 years or older were included in the study, while those with a history of congestive heart failure were excluded from the final analysis.

### 2.3 Patient data

Information about patients, encompassing fundamental demographic details, previous medical history, and specifics regarding chronic conditions like malignant disease, arterial hypertension, diabetes, heart failure, chronic obstructive pulmonary disease, and chronic renal disease, was gathered from the hospital electronic database BIRPIS21 (SRC Infonet, Kranj, Slovenia).

### 2.4 Laboratory

The General Laboratory of our institution conducted the majority of laboratory analyses. Our focus on laboratory data encompassed admission details as well as the most extreme values recorded throughout the entire ICU stay. This included parameters such as the lowest pH, highest partial pressure of carbon dioxide ($pCO_2$), lowest partial pressure of oxygen ($pO_2$), highest D-dimer, highest troponin T, highest procalcitonin (PCT), highest C-reactive protein (CRP), highest creatinine, highest leukocyte count, and others.

### 2.5 Body mass index (BMI)

The weight of each patient was measured at admission using an internal scale system of ICU-certified beds (Progressa ICU Hospital Bed, Hill-Rom Holdings, Illinois, USA). Only admission weight data was used in BMI calculation. The height of each patient was measured at admission using standard tape measure in supine position, from top of the head to the heels. Body Mass Index (BMI) was determined using the standard formula: weight (kg) divided by [height (m)]$^2$. Obesity was defined as a BMI equal to or exceeding 30 kg/m$^2$ [14].

### 2.6 Echocardiography

A transthoracic echocardiographic examination was conducted at admission by the intensive care specialist using a cardiac probe on the GE Vivid S60 Ultrasound machine (GE Healthcare, Chicago, IL, USA). The collected data included left ventricular ejection fraction (LV EF), determined by eyeballing, velocity time integral (VTI) in the left ventricular outflow tract (LVOT), tricuspid annular plane systolic excursion (TAPSE), and maximal inferior vena cava diameter (VCI max). The definitions of left ventricular heart failure were established in accordance with the American Heart Association Guidelines [15].

### 2.7 Treatment

Data regarding treatment was extracted from the intensive care information system (Centricity Critical Care, GE Healthcare, USA). Initially, all patients were administered parenteral methylprednisolone at a dose of 1 mg/kg body weight.

To characterize respiratory support, the following data were collected: instances of self-proning and proning during mechanical ventilation, frequency and duration of high-flow nasal cannula (HFNC) oxygen therapy, non-invasive ventilation (NIV), and invasive mechanical ventilation (IMV). Duration of HFNC and NIV respiratory support was guided by periodically calculated respiratory rate-oxygenation (ROX) index values [16]. For patients on IMV, the following maximal values at any time during treatment were recorded: positive end-expiratory pressure (PEEP), peak inspiratory pressure, and tidal volume.

Documentation also included information on the use of nitric oxide inhalation therapy, norepinephrine, levosimendan, systemic thrombolytic treatment, and renal replacement therapy.

### 2.8 Complications and mortality

Complications data, including ventilator-associated pneumonias, catheter-related bloodstream infections, urosepsis, ICU mortality, and hospital mortality, were gathered.

### 2.9 Definitions

Ventilator-associated pneumonia (VAP) was defined as the presence of new or changing infiltrates on chest X-ray, occurring more than 48 hours after the initiation of IMV, in addition to both of the following criteria: (i) new onset of fever (body temperature $\geq$38 °C) or hypothermia (body temperature $\leq$35 °C) and/or leukocytosis (total peripheral white blood cell (WBC) count $\geq$10,000 cells/$\mu$L) or leukopenia (total peripheral WBC count $\leq$4500 cells/$\mu$L) with >15% immature neutrophils; (ii) new onset of suction respiratory secretions and/or the need for acute changes in ventilatory support parameters to improve oxygenation.

Catheter-related bloodstream infection (CRBSI) was defined as the identification of bacteraemia originating from an intravenous catheter. Microbiological samples were obtained using BacT/ALERT SA (aerobic) and BacT/ALERT

SN (anaerobic) bottles, which were then incubated in the BacT/Alert 3D blood culture instrument (bioMérieux, Ballerup, Denmark).

The diagnosis of fungal infection was made using the established criteria as described previously [17].

### 2.10 Primary outcome

The primary outcomes assessed were mortality at ICU and hospital discharge.

### 2.11 Secondary outcome

The correlation between ICU complications and ICU mortality was analysed as a secondary outcome.

### 2.12 Sample size estimation

It was determined that the sample size of 96 patients (48 in each group) was required to detect statistically significant differences (type I error ($\alpha$) 0.05 and power, type II error ($\beta$) 0.20) in BMI between ICU survivors and non-survivors. This estimation was based on the proportion of survivors (0.60) with BMI >30 kg/m$^2$ and non-survivors (0.40) with BMI 25–30 kg/m$^2$ [18]. Sample size estimation was conducted using MedCalc version 12.5 (MedCalc Software Ltd, Ostend, Belgium).

### 2.13 Statistical analysis

The data were summarized as mean (±standard deviation) for metric variables and as absolute and relative frequencies for categorical variables. The D'Agostino-Pearson test for normal distribution did not reject the null hypothesis stating that variables were normally distributed. Student's *t*-test and Mann-Whitney test for independent samples were employed for metric variables, while Chi-Square was used for categorical data. Multivariate logistic regression modelling (Backward method, enter variable if $p < 0.05$, remove variable if $p > 0.1$), with odds ratio (OR) and 95% confidence interval (95% CI) calculations, was used to test the relationship between ICU/hospital mortality and dichotomous BMI (≥30 kg/m$^2$ as 1, <30 kg/m$^2$ as 0) at admission, age, gender, chronic diseases, C-reactive protein level, lactate at admission and mechanical ventilation at any time during ICU stay. Significant correlations between continuous variables were excluded before inclusion in statistical models. The analyses were conducted using SPSS version 25.0 (SPSS Inc., Chicago, IL, USA) and MedCalc version 12.5 (MedCalc Software Ltd, Ostend, Belgium) software packages. A $p$-value of $< 0.05$ was deemed to indicate statistical significance.

## 3. Results

Out of the 343 patients admitted to our ICU during the study period, 208 individuals under the age of 70 and 28 patients with a history of heart failure were excluded. Body weight at admission was measured for all patients, but height was not measured for 5 patients. A total of 102 patients were included in the final analysis, 51 ICU survivors and 51 non-survivors. The ICU mortality rate in our cohort was 50.0%. The general overview of patients, including their chronic therapy and history, is detailed in Table 1. There was no significant difference in average age between survivors and non-survivors (76 ± 5 years *vs.* 77 ± 5 years, $p = 0.1$). However, the ICU length of stay was shorter in ICU survivors compared to non-survivors (9.1 ± 8.5 days *vs.* 13.6 ± 9.3 days, $p = 0.01$).

Upon admission, there were no discernible differences in vital parameters between survivors and non-survivors. Nevertheless, serum lactate values were notably lower in survivors (2.1 ± 1.6 mmol/L *vs.* 3.7 ± 4.2 mmol/L, $p = 0.012$) (Table 2). Average $PaO_2/FiO_2$ (PF) ratioat admission was 80 ± 52 mmHg; it tends to be higher in ICU survivors compared to non-survivors, although not reaching statistical significance (89 ± 60 mmHg *vs.* 72 ± 43 mmHg, $p = 0.08$).

Lower pH, $pO_2$, and haemoglobin oxygen saturation ($stHbO_2$) values, in contrast to higher leukocyte count, C-reactive protein, D-dimer, and $pCO_2$ values, were observed in ICU non-survivors compared to survivors (Table 2).

All patients received parenteral methylprednisolone. Survivors had a shorter duration of non-invasive ventilation (1.5 ± 0.8 days *vs.* 2.9 ± 2.1 days, $p = 0.01$) and were less frequently subjected to invasive mechanical ventilation (51% *vs.* 84%, $p = 0.001$). No significant differences between groups were observed regarding maximal PEEP and tidal volume values; however, non-survivors exhibited higher recorded maximal peak pressures. Ventilator-associated pneumonia was more frequently detected in mechanically ventilated non-survivors compared to mechanically ventilated survivors (63% (27/43) *vs.* 46% (12/26), $p = 0.049$) (Table 3).

Echocardiograms were conducted for all patients upon admission (Table 4). No group differences were observed in LV EF, systolic VTI LVOT, TAPSE, or maximal VCI diameter measurements.

Fig. 1 illustrates BMI distributions of survivors and non-survivors. BMI was significantly higher in survivors (30.5 ± 5.6 *vs.* 28.1 ± 4.5 kg/m$^2$, $p = 0.02$) (Table 1). A total of 26 (51%) survivors and only 15 (29%) non-survivors had a BMI ≥30 kg/m$^2$ (Chi-square $p = 0.025$).

At admission BMI ≥30 kg/m$^2$, adjusted for gender and chronic diseases, was related to lower ICU (OR: 0.33, 95% CI: 0.12 to 0.95, $p = 0.04$) and hospital (OR: 0.21, 95% CI: 0.05 to 0.82, $p = 0.024$) mortality (Table 5). The requirement for invasive mechanical ventilation at any point during the ICU stay emerged as the most influential predictor of both ICU and hospital mortality. Higher lactate values at admission were associated with hospital mortality (Table 5 and **Supplementary Table 1**).

## 4. Discussion

Our retrospective cohort study showed that higher body weight is protective in elderly critically ill with COVID-19 pneumonia. On the other hand, invasive mechanical ventilation at any time during ICU stay was associated with the worse ICU and hospital outcome. Higher lactate at admission was associated with hospital mortality.

**TABLE 1. Characteristics of patients, previous medical background, and chronic treatment summary.**

| Variable | All n = 102 | ICU survivors n = 51 (50%) | ICU non-survivors n = 51 (50%) | BMI <30 kg/m$^2$ n = 59 (58%) | BMI ≥30 kg/m$^2$ n = 43 (42%) |
|---|---|---|---|---|---|
| Age, years | 77 ± 5 | 76 ± 5 | 77 ± 5 | 76 ± 5 | 77 ± 5 |
| Gender, female/male, n (%) | 27 (26)/75 (74) | 12/39 | 15/36 | 14/45 | 13/30 |
| Height, cm | 173 ± 7 | 173 ± 7 | 173 ± 8 | 173 ± 8 | 172 ± 6 |
| Body weight, kg | 88 ± 16 | 91 ± 17 | 84 ± 14* | 79 ± 12 | 101 ± 14*** |
| BMI, kg/m$^2$ | 29.3 ± 5.2 | 30.5 ± 5.6 | 28.1 ± 4.5* | 26.1 ± 3.0 | 34.2 ± 4.1*** |
| Duration of COVID-19 symptoms, days | 7 ± 4 | 7 ± 4 | 7 ± 4 | 7 ± 4 | 7 ± 3 |
| ICU LOS, days | 11.4 ± 9.2 | 9.1 ± 8.5 | 13.6 ± 9.4* | 13.0 ± 9.6 | 9.7 ± 8.9 |
| Hospital LOS, days | 20.4 ± 10.6 | 21.9 ± 10.2 | 19.0 ± 10.9 | 21.8 ± 10.4 | 19.4 ± 10.3 |
| Previous history: | | | | | |
| Arterial hypertension, n (%) | 72 (71) | 37 (73) | 35 (69) | 43 (72) | 29 (65) |
| Diabetes, n (%) | 36 (35) | 18 (35) | 18 (35) | 19 (32) | 17 (40) |
| COPD, n (%) | 10 (10) | 6 (12) | 4 (8) | 8 (14) | 2 (5) |
| Chronic kidney failure, n (%) | 18 (18) | 8 (16) | 10 (20) | 13 (22) | 5 (12) |
| Therapy at home: | | | | | |
| Statins, n (%) | 19 (19) | 16 (31) | 13 (25) | 16 (27) | 13 (30) |
| Beta-Blocker, n (%) | 41 (40) | 19 (37) | 22 (43) | 18 (31) | 23 (53) |
| Inhaled corticosteroids, n (%) | 13 (13) | 6 (12) | 7 (14) | 11 (19) | 3 (7) |
| ACE inhibitors, n (%) | 43 (42) | 20 (39) | 23 (45) | 22 (37) | 21 (49) |
| Insulin, n (%) | 12 (12) | 6 (12) | 6 (12) | 6 (10) | 6 (14) |
| Aspirin, n (%) | 32 (31) | 17 (33) | 15 (29) | 20 (34) | 12 (28) |
| Diuretics, n (%) | 25 (25) | 14 (27) | 11 (22) | 15 (25) | 10 (23) |

*Data are presented as means accompanied by standard deviations or as counts with corresponding percentages. */ ***Denotes statistically significant difference between ICU survivors and non-survivors or between patient groups with BMI <30 kg/m$^2$ and BMI ≥30 kg/m$^2$ at * < 0.05 and *** < 0.001 level. Abbreviations: ACE, angiotensin-converting enzyme; BMI, Body mass index; COPD, chronic obstructive pulmonary disease; COVID-19, Coronavirus disease 2019; ICU, intensive care unit; LOS, length of stay.*

## 4.1 Obesity and its relationship to mortality

Obesity and overweight nutrition status have been identified as unfavorable outcome predictors for patients infected with novel coronavirus, namely, the higher the BMI, the worse the outcomes in the population of unselected patients [19].

On the other hand, analysis from the SMAtteo COVID-19 REgistry (74 out of 331 patients had BMI >30 kg/m$^2$, average age 67 ± 21 years) supports our results [9]. They asserted that, despite the complex management of obese patients in the ICU, which includes challenges related to ventilation and nursing, obesity should not be considered a definitive predictive factor for an unfavorable outcome in intensive care.

Obesity (mortality hazard ratio (HR): 0.69, 95% CI: 0.09 to 5.29, $p = 0.72$) was also not predictive of COVID-19 associated mortality in elderly patients from a long-term care facility [20].

In 3019 elderly (>65 years) and metabolically unhealthy (defined as metabolic abnormalities including diabetes, hypertension and dyslipidemia) hospitalised patients from Wuhan, China, underweight nutritional status (HR: 4.58, 95% CI: 1.56 to 13.48, $p = 0.03$) and obesity (HR: 6.49, 95% CI: 2.35 to 17.95, $p = 0.001$) have been associated with COVID-19 mortality [21]. Notably, overweight nutritional status was not associated with mortality in either metabolically healthy or metabolically unhealthy elderly patients.

Our study observed a U-shaped curve association between BMI and COVID-19 mortality, which is consistent with findings from a study involving 10,861 adult patients with SARS-CoV-2 infection in New York, along with other smaller studies [22, 23]. The findings in the report by Kompaniyets L. *et al.* [24] suggest that overweight and obesity are risk factors for invasive mechanical ventilation. Additionally, obesity or severe obesity are identified as risk factors for hospitalization, ICU admission, and death among patients aged ≥65 years. However, the U-curve (or J-shaped curve) for predicting ICU mortality in patients aged >75 years has been almost flat, indicating no influence of BMI on the mortality of elderly population [24].

**TABLE 2. Clinical parameters at admission and treatment-related laboratory findings.**

| Variable | All n = 102 | ICU survivors n = 51 (50%) | ICU non-survivors n = 51 (50%) | BMI <30 kg/m$^2$ n = 59 (58%) | BMI ≥30 kg/m$^2$ n = 43 (42%) |
|---|---|---|---|---|---|
| Heart rate at admission, bpm | 90 ± 25 | 88 ± 25 | 92 ± 25 | 90 ± 25 | 89 ± 23 |
| Respiratory rate at admission, rpm | 30 ± 9 | 29 ± 7 | 32 ± 10 | 32 ± 7 | 32 ± 7 |
| SAP at admission, mmHg | 139 ± 28 | 141 ± 28 | 137 ± 28 | 141 ± 30 | 138 ± 25 |
| DAP at admission, mmHg | 68 ± 15 | 68 ± 16 | 68 ± 15 | 68 ± 15 | 68 ± 15 |
| Highest $FiO_2$, % | 93 ± 19 | 91 ± 21 | 95 ± 15 | 94 ± 16 | 91 ± 21 |
| Worst pH | 7.26 ± 0.14 | 7.34 ± 0.09 | 7.17 ± 0.13** | 7.24 ± 0.16 | 7.27 ± 0.12 |
| Lowest $pO_2$, kPa | 7.26 ± 1.76 | 8.31 ± 3.93 | 7.00 ± 1.21*** | 7.52 ± 1.60 | 7.95 ± 1.96 |
| Highest $pCO_2$, kPa | 8.59 ± 3.58 | 6.78 ± 2.51 | 10.40 ± 3.59*** | 8.89 ± 3.56 | 8.46 ± 3.72 |
| Highest $HCO_3$, mmol/L | 30.0 ± 6.8 | 29.1 ± 6.1 | 30.9 ± 7.1 | 31.0 ± 6.5 | 29.1 ± 7.1 |
| Lowest $StHbO_2$, % | 89.4 ± 7.4 | 91.0 ± 5.6 | 79.1 ± 7.9*** | 88.9 ± 7.6 | 90.5 ± 6.0 |
| Lactate at admission, mmol/L | 2.9 ± 3.2 | 2.1 ± 1.6 | 3.8 ± 4.2* | 2.9 ± 3.8 | 2.7 ± 1.9*** |
| Highest Creatinine, µmol/L | 219 ± 193 | 175 ± 174 | 265 ± 204 | 226 ± 207 | 187 ± 122*** |
| Highest proBNP, pg/mL† | 13,575 ± 12,584 (n = 16) | 6803 ± 6735 (n = 8) | 20,346 ± 13,754* (n = 8) | 15,920 ± 13,671 (n = 8) | 1102 ± 12,756 (n = 8) |
| Highest Troponin I, ng/mL† | 436 ± 1517 (n = 75) | 588 ± 2071 (n = 43) | 284 ± 570** (n = 32) | 451 ± 1504 (n = 43) | 200 ± 197** (n = 32) |
| Highest D-dimer, µg/L† | 10,244 ± 10,542 (n = 89) | 6676 ± 8251 (n = 43) | 13,580 ± 11,313* (n = 46) | 10,779 ± 9875 (n = 51) | 9028 ± 11,293 (n = 37) |
| Highest PCT, ng/L | 7.74 ± 17.2 | 5.93 ± 17.13 | 9.51 ± 19.12 | 11.19 ± 23.56 | 3.69 ± 6.01*** |
| Highest CRP, mg/L | 216 ± 125 | 177 ± 108 | 256 ± 130*** | 223 ± 130 | 208 ± 123 |
| Highest leucocyte count, $10^9$/L | 21.6 ± 22.3 | 17.5 ± 17.7 | 28.3 ± 25.2* | 24.8 ± 24.8 | 20.1 ± 20.2 |
| Highest thrombocyte count, $10^9$/L | 276 ± 173 | 289 ± 174 | 264 ± 172 | 298 ± 193 | 253 ± 145 |
| Highest AST, µkat/L | 4.2 ± 11.3 | 2.2 ± 5.9 | 6.4 ± 15.2*** | 4.9 ± 13.8 | 3.2 ± 6.8** |
| Highest ALT, µkat/L | 2.8 ± 6.5 | 1.6 ± 2.2 | 3.3 ± 6.7*** | 2.7 ± 6.0 | 1.9 ± 2.7** |

*Data are presented as means accompanied by standard deviations. †Numbers in brackets represent number of patients that had that measurement done. */ **/ ***Denotes statistically significant difference between ICU survivors and non-survivors or between patient groups with BMI <30 kg/m$^2$ and BMI ≥30 kg/m$^2$ at * < 0.05, ** < 0.01 and *** < 0.001 level. Abbreviations: ALT, alanine transaminase; AST, aspartate aminotransferase; BMI, body mass index; BNP, brain natriuretic peptide; CRP, C-reactive protein; DAP, diastolic arterial pressure; $FiO_2$, fraction of inspired oxygen; $HCO_3$, hydrogen bicarbonate; ICU, intensive care unit; $pCO_2$, partial pressure of carbon dioxide; PCT, procalcitonin; $pO_2$, partial pressure of oxygen; SAP, systolic arterial pressure; $StHbO_2$, oxygen saturation.*

In a recent study involving 222 patients (mean age of 62.4 ± 12 years), individuals with moderate obesity (BMI 30–39.9 kg/m$^2$) exhibited a lower mortality rate compared to patients with normal weight, overweight, or severe obesity [4]. Consistent with these findings are results of Japanese study that confirmed protective effect of higher BMI [25].

Obesity paradox presents a paradox within the paradox [26]. This phenomenon could be elucidated by a potentially protective role of excess adipose tissue, creating a more favorable environment to endure a substantial reduction in the patient's caloric intake, which is frequently encountered in intensive care settings, such as sepsis or ventilator-induced lung injury [27]. Nevertheless, it is important to acknowledge the limitations of a blind BMI classification, as it is unable to distinguish between muscle mass and adipose tissue.

Another plausible explanation for the paradox is that clinicians might perceive patients with obesity as being at a higher risk for adverse outcomes, leading to their earlier admission,

**TABLE 3. Respiratory support, treatment modalities and complications.**

| Variable | All n = 102 | ICU survivors n = 51 (50%) | ICU non-survivors n = 51 (50%) | BMI <30 kg/m$^2$ n = 59 (58%) | BMI ≥30 kg/m$^2$ n = 43 (42%) |
|---|---|---|---|---|---|
| Respiratory support | | | | | |
| Self-proning, n (%) | 2 (2) | 1 (2) | 1 (2) | 1 (2) | 1 (2) |
| High-flow, n (%) | 34 (33) | 14 (27) | 20 (39) | 21 (36) | 12 (28) |
| High-flow duration, days | 2.3 ± 1.6 | 2.4 ± 2.2 | 2.3 ± 1.2 | 2.3 ± 1.6 | 2.3 ± 1.9 |
| NIV, n (%) | 36 (35) | 16 (31) | 20 (39) | 21 (36) | 16 (37) |
| NIV duration, days | 2.3 ± 1.8 | 1.5 ± 0.8 | 2.9 ± 2.1* | 2.5 ± 1.8 | 1.9 ± 1.7 |
| IMV, n (%) | 69 (68) | 26 (51) | 43 (84)*** | 43 (73) | 26 (60) |
| IMV duration, days | 10.8 ± 8.8 | 8.1 ± 8.6 | 12.4 ± 8.6 | 12.3 ± 8.7 | 9.7 ± 9.2 |
| Proning during IMV, n (%) | 15 (15) | 4 (8) | 11 (22) | 7 (12) | 8 (17) |
| Maximal PEEP, cm$H_2O$ | 12 ± 4 | 11 ± 4 | 13 ± 4 | 12 ± 3 | 13 ± 4 |
| Tidal volume, mL | 534 ± 104 | 559 ± 93 | 520 ± 108 | 537 ± 109 | 528 ± 97 |
| Max Peak pressure, cm$H_2O$ | 35 ± 7 | 32 ± 7 | 37 ± 6** | 36 ± 6 | 35 ± 7 |
| Specific treatments | | | | | |
| Methylprednisolone, n (%) | 102 (100) | 51 (100) | 51 (100) | 59 (100) | 43 (100) |
| Levosimendan, n (%) | 12 (12) | 10 (20) | 2 (4) | 4 (8) | 7 (16) |
| Nitric oxide inhalation, n (%) | 2 (2) | 2 (4) | 0 | 2 (3) | 0 |
| Thrombolysis (rTPA), n (%) | 2 (2) | 0 | 2 (4) | 0 | 2 (5) |
| Renal replacement therapy, n (%) | 17 (17) | 13 (25) | 4 (8)* | 11 (17) | 6 (14) |
| Maximal noradrenalin, µg/kg/min | 0.71 ± 0.46 | 0.55 ± 0.50 | 0.86 ± 0.35*** | 0.75 ± 0.44 | 0.64 ± 0.49 |
| Dexmedetomidine, n (%) | 27 (53) | 13 (25) | 14 (27) | 20 (34) | 7 (16) |
| Complications | | | | | |
| VAP, n (%) | 39 (39) | 12 (24) | 27 (53)** | 24 (41) | 15 (35) |
| Catheter sepsis, n (%) | 1 (1) | 0 | 1 (2) | 1 (2) | 0 |
| Urosepsis, n (%) | 24 (24) | 13 (25) | 11 (22) | 15 (25) | 9 (21) |
| Fungal infection, n (%) | 35 (34) | 13 (25) | 21 (41) | 22 (37) | 13 (30) |

*Data are presented as means accompanied by standard deviations or as counts with corresponding percentages. */ **/ ***Denotes statistically significant difference between ICU survivors and non-survivors or between patient groups with BMI <30 kg/m$^2$ and BMI ≥30 kg/m$^2$ at * < 0.05, ** < 0.01 and *** < 0.001 level. Abbreviations: BMI, Body mass index; ICU, intensive care unit; IMV, invasive mechanical ventilation; NIV, non-invasive mechanical ventilation; PEEP, positive end-expiratory pressure; VAP, ventilator associated pneumonia.*

**TABLE 4. Echocardiographic parameters of our cohort.**

| Variable | All n = 102 | ICU survivors n = 51 (50%) | ICU non-survivors n = 51 (50%) | BMI <30 kg/m$^2$ n = 59 (58%) | BMI ≥30 kg/m$^2$ n = 43 (42%) |
|---|---|---|---|---|---|
| LV EF, % | 51 ± 15 | 49 ± 14 | 52 ± 15 | 52 ± 15 | 49 ± 13 |
| LVOT VTI, cm | 19 ± 5 | 18 ± 5 | 19 ± 4 | 20 ± 4 | 18 ± 5 |
| TAPSE, cm | 2.0 ± 0.5 | 1.9 ± 0.6 | 2.0 ± 0.5 | 2.0 ± 0.5 | 2.0 ± 0.5 |
| VCI max. diameter, cm | 2.0 ± 0.5 | 2.2 ± 0.5 | 1.9 ± 0.5 | 2.1 ± 0.5 | 2.0 ± 0.6 |

*Values represent means with standard deviations. Abbreviations: BMI, Body mass index; ICU, intensive care unit; LV EF, left ventricular ejection fraction; LVOT VTI, left ventricular outflow tract velocity time integral; TAPSE, tricuspid annular plane systolic excursion; VCI, vena cava inferior.*

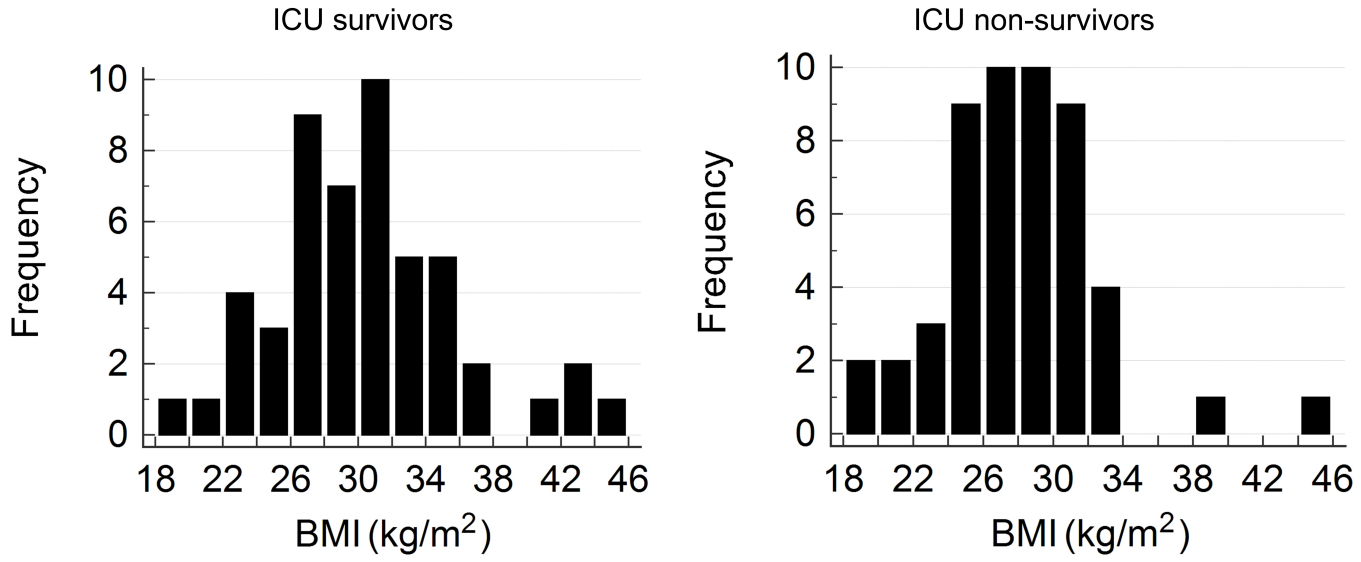


**FIGURE 1. BMI distribution in ICU survivors (left) and non-survivors (right).** Survivors exhibited a higher BMI compared to non-survivors (30.5 ± 5.6 *vs.* 28.1 ± 4.5 kg/m$^2$, $p = 0.02$). Abbreviation: BMI, body mass index.

**TABLE 5. Multivariate logistic regression models, backward method.**

| Variable in the model | OR | 95% CI | Statistics ($p$) |
|---|---|---|---|
| Logistic regression model of ICU mortality[1] (Full model − 2 Log Likelihood = 97.2, Chi-square $p < 0.001$) | | | |
| Age, years | 1.099 | 0.986–1.225 | 0.087 |
| BMI (≥30 kg/m$^2$ = 1, <30 kg/m$^2$ = 0) | 0.332 | 0.116–0.952 | 0.043* |
| Lactate, mmol/L | 1.442 | 0.988–2.105 | 0.058 |
| Mechanical ventilation (Yes = 1, No = 0) | 7.007 | 2.068–23.743 | 0.001* |
| Logistic regression model of hospital mortality[2] (Full model − 2 Log Likelihood = 67.9, Chi-square $p < 0.001$) | | | |
| Age, years | 1.163 | 1.009–1.341 | 0.038* |
| BMI (≥30 kg/m$^2$ = 1, <30 kg/m$^2$ = 0) | 0.211 | 0.055–0.815 | 0.024* |
| Lactate, mmol/L | 3.482 | 1.644–7.373 | 0.001* |
| Mechanical ventilation (Yes = 1, No = 0) | 9.449 | 2.032–43.936 | 0.004* |
| History of arterial hypertension (Yes = 1, No = 0) | 0.284 | 0.075–1.083 | 0.065 |

*Values are expressed as odds ratios along with corresponding 95% confidence intervals. *Indicates a statistically significant difference between groups at the <0.05 level. [1] Variables tested, but in the model (age, C-reactive protein at admission, history of chronic kidney failure, chronic obstructive pulmonary disease, arterial hypertension). [2] Variables tested, but in the model (age, C-reactive protein at admission, history of chronic kidney failure, chronic obstructive pulmonary disease). Abbreviations: BMI, body mass index; CI, confidence interval; ICU, intensive care unit; OR, odds ratio.*

more assertive and timely medical interventions [28].

The obesity paradox in patients with ARDS has been the subject of exploration in numerous studies and two recent meta-analyses [13, 29]. In the study conducted by Ni and colleagues [13], which involved the analysis of evidence pertaining to the association between BMI and clinical outcomes in 6268 ARDS patients, the authors concluded that both obesity and morbid obesity were associated with a lower mortality rate in individuals with ARDS, thus supporting the concept of the obesity paradox. In a separate analysis that included four additional studies, Zhi *et al.* [29] reported that obesity heightened ARDS-associated morbidity in the ICU population; nonetheless, mortality due to ARDS was lower in obese patients compared to non-obese individuals.

The prevalence of obesity and its impact on outcomes in patients with COVID-19 were evaluated in a recent systematic review and meta-analysis, which included 19 studies [30]. Obesity was not found to be associated with a higher risk of mortality, potentially attributable to the obesity survival paradox and/or unidentified factors.

As age increases, the association between the obesity paradox and mortality appears to strengthen [31]. Some recent studies have reported similar findings [12, 32]. For instance, Fukuoka *et al.* [12] identified a significant obesity paradox among older patients (aged ≥70 years) but did not observe a similar phenomenon among younger patients with acute my-

ocardial infarction after percutaneous coronary intervention. They proposed two potential explanations for this finding. Firstly, elderly patients with higher BMI are expected to be more resilient to the deleterious effects of obesity than younger patients, potentially due to survival bias [12]. Secondly, older patients may have a higher composition of adipose tissue than younger patients with the same BMI [33], reinforcing the association between BMI and mortality.

The obesity paradox extends beyond a mere association between BMI and mortality, underscoring the significance of illness severity in understanding this complex phenomenon. Lactate is a well-known indicator of the severity of acute circulatory failure [34]. In our study, non-survivors exhibited more severe circulatory/respiratory failure (as evidenced by higher lactate levels at admission), and a greater need for invasive mechanical ventilation at any time during ICU stay. In the multivariate logistic regression model, lactate and need for invasive mechanical ventilation were positively associated, while BMI was negatively related to hospital mortality. In a previous study, the mortality benefit that was adjusted for in patients with higher BMI was found to be diminished in those with elevated lactate levels. No mortality benefit was observed in higher BMI categories when lactate levels exceeded 5 mmol/L [35].

Other authors maintain a skeptical stance and offer methodological explanations to elucidate the obesity paradox, such as different types of bias, namely confounding or selection bias [36]. The first potential type of bias is confounding bias, which can arise, particularly as a consequence of reverse causation. In this scenario, pre-existing disease results in unintended weight loss and higher mortality, creating an illusion of obesity being protective [37].

Other potential types of bias involve BMI group misallocation, especially when estimating rather than actually measuring height and weight in critically ill patients, (both were measured at admission in our study) [38]. Additionally, treatment biases may occur due to closer monitoring and different treatment approaches for obese patients [39].

### 4.2 Mortality rates in elderly patients with severe or critical COVID-19 pneumonia

Both age and frailty exhibit independent associations with adverse outcomes in individuals with COVID-19 [40]. The mortality rate among elderly patients following admission to the intensive care unit for COVID-19, as reported in a recent study [41], was comparable to the mortality observed in our cohort. Notably, our study was conducted during the second surge of COVID-19 in Europe, a period characterized by higher mortality rates among critically ill elderly patients compared to the initial surge [42].

We have included only elderly critically ill, analyzed based on BMI. The important point that our research did not directly explore is influence of age. Researches of large retrospective study in Spain [43] that included 5746 patients, found that obesity was negatively correlated with negative outcomes in patients aged 65 years or younger, but did not identify the same in older patients. The study was not limited to ICU setting. Furthermore, Graziano *et al.* [44] did not find abdominal adiposity to be associated with ICU admissions or mortality in 195 non-critically ill patients with mean age of 71 years. Similarly, BMI was only associated with increased in-hospital mortality in patients aged 50 years or younger in study conducted by Hendren *et al.* [23] in association with American Heart Association registry data. Reported data further indicate that obesity paradox could be limited to elderly patients with COVID-19 pneumonia and is not applicable to younger patients.

Consistent with our study, nosocomial infections were already identified as a significant risk factor for mortality (OR: 7.86, 95% CI: 2.16 to 28.57, $p = 0.002$) of elderly (mean age 72 years) patients hospitalized with COVID-19 in Korea [45] as is also true in younger patients [46].

### 4.3 Limitations of our study

This study was designed as a cohort study, utilizing a complete sample from a single center, and it involved the utilization of data from ICU admission to the hard endpoint of mortality or discharge. Nevertheless, this study had the following limitations. Firstly, our study only analyses elderly critically ill patients with COVID-19 pneumonia. Results thus might not be generalizable to all age groups. Secondly, retrospective design of our study did not allow assessment of body weight changes during ICU stay. Thirdly, our study was not designed to determine basal level of sarcopenia and frailty status of our cohort, which is important in elderly [47]. Fourthly, we gathered all data during the hospitalization period and did not perform a long-term follow-up after discharge. Fifthly, the reversal causality could not be completely ruled out. Lastly, the limited number of included patients has hindered the feasibility of conducting complex statistical modeling.

## 5. Conclusions

Our retrospective cohort study, encompassing elderly critically ill patients with severe or critical COVID-19 pneumonia, affirms that individuals with a higher BMI at admission exhibit a lower mortality rate and a shorter ICU length of stay, implicating the obesity paradox. Additionally, lower lactate levels upon admission and the absence of a requirement for invasive mechanical ventilation at any point during the ICU stay are both independently associated with a lower mortality rate. In crowded ICUs, especially during epidemics, the decision-making process of admitting elderly patients with severe cardiovascular/respiratory or other organ failure poses a significant challenge. Our study contributes a small piece to the complex mosaic of treating elderly critically ill patients.

## ABBREVIATIONS

ACE, angiotensin-converting enzyme; ALT, alanine transaminase; ARDS, acute respiratory distress syndrome; AST, aspartate aminotransferase; BMI, body mass index; BNP, brain natriuretic peptide; CI, confidence interval; COPD, chronic obstructive pulmonary disease; COVID-19, Coronavirus disease 2019; CRBSI, catheter-related bloodstream infection; CRP, C-reactive protein; EF, ejection fraction; $FiO_2$, fraction of

inspired oxygen; HFNC, high-flow nasal cannula; HR, hazard ratio; ICU, intensive care unit; IMV, invasive mechanical ventilation; LOS, length of stay; LUS, lung ultrasound; LV, left ventricle; LVOT, left ventricular outflow tract; NIV, non-invasive mechanical ventilation; OR, odds ratio; $pCO_2$, partial arterial carbon dioxide pressure; PCT, pro-calcitonin; PEEP, positive end-expiratory pressure; $pO_2$, partial arterial oxygen pressure; rTPA, recombinant tissue plasminogen activator; RT-PCR, real-time polymerase chain reaction; SAP, systolic arterial pressure; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; $StHbO_2$, oxygen saturation; TAPSE, tricuspid annular plane systolic excursion; VAP, ventilator-associated pneumonia; VTI, velocity time integral; VCI, vena cava inferior; WBC, white blood cell.

## AVAILABILITY OF DATA AND MATERIALS

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

## AUTHOR CONTRIBUTIONS

HB, MK and MP—have given substantial contribution to the conception of the design of the study. HB, MK and AV—to acquisition. PK and MP—to analysis and interpretation of the data. MP—as department head supervised all personnel for employing good clinical practices in day-to-day work, data collection, maintaining patient's privacy and article production. All authors have participated to drafting and revising the manuscript. All authors have approved the submitted version and have agreed both to be personally accountable for the author's own contributions and to ensure that questions related to the accuracy or integrity of any part of the work, even ones in which the author was not personally involved, are appropriately investigated, resolved, and the resolution documented in the literature. All authors read and approved the final manuscript.

## ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was conducted according to the guidelines of the Declaration of Helsinki. It was approved by the Republic of Slovenia National Medical Ethics Committee (No. 0120-168/2021/7, 22 July 2021) and Institutional Review Board of General Hospital Celje (No. 17/KS/2021-1, 05 March 2021). Data collection and analysis were undertaken after all approvals were granted. Patient consent was waived due to retrospective nature of the study.

## ACKNOWLEDGMENT

The authors would like to acknowledge the importance of nurses, physiotherapy team and all supportive teams for treatment of our patients. Our thanks to all members of Celje COVID-study group: Parežnik R., Hudournik B., Mežnar M., Valović J., Gulan M., Žgavc B., Gabršček Parežnik L., Triller K., Kolenc A., Kotnik G., Majcen M., Kolenc Dolinar M., Kosi M., Skočir A., Ban B., Štern S., Kalušević D., Mazi P., Berlec M., Jagodič Korošec H., Lalić D., Kus A., Parežnik Slatinek A., Lazić J, Globočnik Šali M., Brecl E., Tumpaj T., Sajovic E., Vajdl T, Tacar P, Markoska M.

## FUNDING

This research received no external funding.

## CONFLICT OF INTEREST

The authors declare no conflict of interest. Matej Podbregar is serving as one of the Editorial Board members of this journal. We declare that Matej Podbregar had no involvement in the peer review of this article and has no access to information regarding its peer review. Full responsibility for the editorial process for this article was delegated to GM.

## SUPPLEMENTARY MATERIAL

Supplementary material associated with this article can be found, in the online version, at https://oss.signavitae.com/mre-signavitae/article/1810195179239292928/attachment/Supplementary%20material.docx.

## REFERENCES

[1] World Health Organization. Obesity and overweight. 2021. Available at: https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight (Accessed: 30 December 2021).

[2] Aghili SMM, Ebrahimpur M, Arjmand B, Shadman Z, Pejman Sani M, Qorbani M, *et al*. Obesity in COVID-19 era, implications for mechanisms, comorbidities, and prognosis: a review and meta-analysis. International Journal of Obesity. 2021; 45: 998–1016.

[3] Kooistra EJ, de Nooijer AH, Claassen WJ, Grondman I, Janssen NAF, Netea MG, *et al*. A higher BMI is not associated with a different immune response and disease course in critically ill COVID-19 patients. International Journal of Obesity. 2021; 45: 687–694.

[4] Dana R, Bannay A, Bourst P, Ziegler C, Losser M, Gibot S, *et al*. Obesity and mortality in critically ill COVID-19 patients with respiratory failure. International Journal of Obesity. 2021; 45: 2028–2037.

[5] Dessie ZG, Zewotir T. Mortality-related risk factors of COVID-19: a systematic review and meta-analysis of 42 studies and 423,117 patients. BMC Infectious Diseases. 2021; 21: 855.

[6] Yates T, Zaccardi F, Islam N, Razieh C, Gillies CL, Lawson CA, *et al*. Obesity, chronic disease, age, and in-hospital mortality in patients with covid-19: analysis of ISARIC clinical characterisation protocol UK cohort. BMC Infectious Diseases. 2021; 21: 717.

[7] Chu Y, Yang J, Shi J, Zhang P, Wang X. Obesity is associated with increased severity of disease in COVID-19 pneumonia: a systematic review and meta-analysis. European Journal of Medical Research. 2020; 25: 64.

[8] Luzi L, Radaelli MG. Influenza and obesity: its odd relationship and the lessons for COVID-19 pandemic. Acta Diabetologica. 2020; 57: 759–764.

[9] Biscarini S, Colaneri M, Ludovisi S, Seminari E, Pieri TC, Valsecchi P, *et al*. The obesity paradox: analysis from the SMAtteo COvid-19 REgistry (SMACORE) cohort. Nutrition, Metabolism and Cardiovascular Diseases. 2020; 30: 1920–1925.

[10] Arulanandam B, Beladi H, Chakrabarti A. Obesity and COVID-19 mortality are correlated. Scientific Reports. 2023; 13: 5895.

[11] Halasz G, Leoni MLG, Villani GQ, Nolli M, Villani M. Obesity, overweight and survival in critically ill patients with SARS-CoV-2

pneumonia: is there an obesity paradox? Preliminary results from Italy. European Journal of Preventive Cardiology. 2021; 28: e15–e17.

[12] Fukuoka S, Kurita T, Dohi K, Masuda J, Seko T, Tanigawa T, *et al*. Untangling the obesity paradox in patients with acute myocardial infarction after primary percutaneous coronary intervention (detail analysis by age). International Journal of Cardiology. 2019; 289: 12–18.

[13] Ni Y, Luo J, Yu H, Wang Y, Hu Y, Liu D, *et al*. Can body mass index predict clinical outcomes for patients with acute lung injury/acute respiratory distress syndrome? A meta-analysis. Critical Care. 2017; 21: 36.

[14] Jensen MD, Ryan DH, Apovian CM, Ard JD, Comuzzie AG, Donato KA, *et al*. 2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American college of cardiology/American heart association task force on practice guidelines and the obesity society. Circulation. 2014; 129: S102–S138.

[15] Konstam MA, Kiernan MS, Bernstein D, Bozkurt B, Jacob M, Kapur NK, *et al*. Evaluation and management of right-sided heart failure: a scientific statement from the American Heart Association. Circulation. 2018; 137: e578–e622.

[16] Roca O, Messika J, Caralt B, García-de-Acilu M, Sztrymf B, Ricard J, *et al*. Predicting success of high-flow nasal cannula in pneumonia patients with hypoxemic respiratory failure: the utility of the ROX index. Journal of Critical Care. 2016; 35: 200–205.

[17] Miller JM, Binnicker MJ, Campbell S, Carroll KC, Chapin KC, Gilligan PH, *et al*. A guide to utilization of the microbiology laboratory for diagnosis of infectious diseases: 2018 update by the infectious diseases society of America and the American society for microbiology. Clinical Infectious Diseases. 2018; 67: e1–e94.

[18] Liu Y, Song M, Huang L, Zhu G. "Obesity Paradox" in acute respiratory distress syndrome among patients undergoing cardiac surgery: a retrospective study. Medical Science Monitor. 2021; 27: e931808.

[19] de Siqueira JVV, Almeida LG, Zica BO, Brum IB, Barceló A, de Siqueira Galil AG. Impact of obesity on hospitalizations and mortality, due to COVID-19: a systematic review. Obesity Research & Clinical Practice. 2020; 14: 398–403.

[20] Trecarichi EM, Mazzitelli M, Serapide F, Pelle MC, Tassone B, Arrighi E, *et al*. Clinical characteristics and predictors of mortality associated with COVID-19 in elderly patients from a long-term care facility. Scientific Reports. 2020; 10: 20834.

[21] Zeng J, Liu X, Wang S, Yang S, Jia W, Han K, *et al*. The association between BMI and metabolically unhealthy status with COVID-19 mortality: based on 3019 inpatients from Wuhan, China. Nutrition, Metabolism and Cardiovascular Diseases. 2021; 31: 3219–3226.

[22] Kim TS, Roslin M, Wang JJ, Kane J, Hirsch JS, Kim EJ. BMI as a risk factor for clinical outcomes in patients hospitalized with COVID-19 in New York. Obesity. 2021; 29: 279–284.

[23] Hendren NS, de Lemos JA, Ayers C, Das SR, Rao A, Carter S, *et al*. Association of body mass index and age with morbidity and mortality in patients hospitalized with COVID-19: results from the American Heart Association COVID-19 cardiovascular disease registry. Circulation. 2021; 143: 135–144.

[24] Kompaniyets L, Goodman AB, Belay B, Freedman DS, Sucosky MS, Lange SJ, *et al*. Body mass index and risk for COVID-19-related hospitalization, intensive care unit admission, invasive mechanical ventilation, and death—United States, March–December 2020. Morbidity and Mortality Weekly Report. 2021; 70: 355–361.

[25] Yoshida J, Setoguchi K, Shiraishi K, Kikuchi T, Tanaka M. The obesity paradox in Japanese COVID-19 patients. International Journal of Medical Sciences. 2023; 20: 1508–1512.

[26] Ball L, Serpa Neto A, Pelosi P. Obesity and survival in critically ill patients with acute respiratory distress syndrome: a paradox within the paradox. Critical Care. 2017; 21: 114.

[27] Jose RJ, Manuel A. Does coronavirus disease 2019 disprove the obesity paradox in acute respiratory distress syndrome? Obesity. 2020; 28: 1007.

[28] Anderson MR, Shashaty MGS. Impact of obesity in critical illness. Chest. 2021; 160: 2135–2145.

[29] Zhi G, Xin W, Ying W, Guohong X, Shuying L. "Obesity Paradox" in acute respiratory distress syndrome: a systematic review and meta-analysis. PLOS ONE. 2016; 11: e0163677.

[30] Helvaci N, Eyupoglu ND, Karabulut E, Yildiz BO. Prevalence of obesity and its impact on outcome in patients with COVID-19: a systematic review and meta-analysis. Frontiers in Endocrinology. 2021; 12: 598249.

[31] Lu L, Lu Y, Gao C, Zhang N. Age moderates the relationships between obesity, glucose variability, and intensive care unit mortality: a retrospective cohort study. Journal of Intensive Care. 2021; 9: 68.

[32] Zhou D, Li Z, Shi G, Zhou J. Obesity paradox for critically ill patients may be modified by age: a retrospective observational study from one large database. Critical Care. 2020; 24: 425.

[33] Akazawa N, Kishi M, Hino T, Tsuji R, Tamura K, Hioka A, *et al*. Relationship between aging and intramuscular adipose tissue in older inpatients. Journal of the American Medical Directors Association. 2021; 22: 1287–1291.e1.

[34] Weil MH, Afifi AA. Experimental and clinical studies on lactate and pyruvate as indicators of the severity of acute circulatory failure (shock). Circulation. 1970; 41: 989–1001.

[35] Jagan N, Morrow LE, Walters RW, Plambeck RW, Wallen TJ, Patel TM, *et al*. Sepsis and the obesity paradox: size matters in more than one way. Critical Care Medicine. 2020; 48: e776–e782.

[36] Decruyenaere A, Steen J, Colpaert K, Benoit DD, Decruyenaere J, Vansteelandt S. The obesity paradox in critically ill patients: a causal learning approach to a casual finding. Critical Care. 2020; 24: 485.

[37] Banack HR, Kaufman JS. Estimating the time-varying joint effects of obesity and smoking on all-cause mortality using marginal structural models. American Journal of Epidemiology. 2016; 183: 122–129.

[38] Toft-Petersen AP, Wulff J, Harrison DA, Ostermann M, Margarson M, Rowan KM, *et al*. Exploring the impact of using measured or estimated values for height and weight on the relationship between BMI and acute hospital mortality. Journal of Critical Care. 2018; 44: 196–202.

[39] Schetz M, De Jong A, Deane AM, Druml W, Hemelaar P, Pelosi P, *et al*. Obesity in the critically ill: a narrative review. Intensive Care Medicine. 2019; 45: 757–769.

[40] Geriatric Medicine Research C, Covid C, Welch C. Age and frailty are independently associated with increased COVID-19 mortality and increased care needs in survivors: results of an international multi-centre study. Age Ageing. 2021; 50: 617–630.

[41] Guillon A, Laurent E, Godillon L, Kimmoun A, Grammatico-Guillon L. Long-term mortality of elderly patients after intensive care unit admission for COVID-19. Intensive Care Medicine. 2021; 47: 710–712.

[42] Jung C, Fjolner J, Bruno RR, Wernly B, Artigas A, Bollen Pinto B, *et al*. Differences in mortality in critically ill elderly patients during the second COVID-19 surge in Europe. Critical Care. 2021; 25: 344.

[43] Pepe M, Maroun-Eid C, Romero R, Arroyo-Espliguero R, Fernàndez-Rozas I, Aparisi A, *et al*. Clinical presentation, therapeutic approach, and outcome of young patients admitted for COVID-19, with respect to the elderly counterpart. Clinical and Experimental Medicine. 2021; 21: 249–268.

[44] Graziano E, Peghin M, De Martino M, De Carlo C, Da Porto A, Bulfone L, *et al*. The impact of body composition on mortality of COVID-19 hospitalized patients: a prospective study on abdominal fat, obesity paradox and sarcopenia. Clinical Nutrition ESPEN. 2022; 51: 437–444.

[45] Lee JY, Kim HA. Huh K, Hyun M, Rhee JY, Jang S, *et al*. Risk factors for mortality and respiratory support in elderly patients hospitalized with COVID-19 in Korea. Journal of Korean Medical Science. 2020; 35: e223.

[46] Bardi T, Pintado V, Gomez-Rojo M, Escudero-Sanchez R, Azzam Lopez A, Diez-Remesal Y, *et al*. Nosocomial infections associated to COVID-19 in the intensive care unit: clinical characteristics and outcome. European Journal of Clinical Microbiology & Infectious Diseases. 2021; 40: 495–502.

[47] Riesgo H, Castro A, Del Amo S, San Ceferino MJ, Izaola O, Primo D, *et al*. Prevalence of risk of malnutrition and risk of sarcopenia in a reference hospital for COVID-19: relationship with mortality. Annals of Nutrition and Metabolism. 2021: 77: 324–329.

**How to cite this article:** Marko Kurnik, Helena Božič, Anže Vindišar, Petra Kolar, Matej Podbregar. Protective effect of high body mass index in elderly critically ill with severe COVID-19 pneumonia. Signa Vitae. 2024; 20(7): 43-52. doi: 10.22514/sv.2024.082.