Turk J Intensive Care
DOI: 10.4274/tybd.galenos.2022.92905

ORIGINAL RESEARCH / *ÖZGÜN ARAŞTIRMA*

Özlem Öner,
Begüm Ergan,
Mehmet Çağatay Gürkök,
Murat Küçük,
Oya Özlem Eren-Kutsoylu,
Erdem Yaka,
Ali Necati Gökmen

Is There a Relationship Between Mortality Rates and Nutritional Factors in Critical Ill Patients with COVID-19?

COVID-19'lu Kritik Hastalardaki Ölüm Oranları ile Beslenme Faktörleri Arasında Bir İlişki Var mıdır?

Received/Geliş Tarihi : 04.04.2022
Accepted/Kabul Tarihi : 11.08.2022

Özlem Öner, Necati Gökmen
Dokuz Eylül University Faculty of Medicine, Department of Anesthesiology and Reanimation, Division of Intensive Care, İzmir, Turkey

Begüm Ergan
Dokuz Eylül University Faculty of Medicine, Department of Pulmonary, Division of Intensive Care, İzmir, Turkey

Mehmet Çağatay Gürkök
Dokuz Eylül University Faculty of Medicine, Department of General Surgery, Division of Intensive Care, İzmir, Turkey

Murat Küçük
Dokuz Eylül University Faculty of Medicine, Department of Internal Medicine, Division of Intensive Care, İzmir, Turkey

Oya Özlem Eren-Kutsoylu
Dokuz Eylül University Faculty of Medicine, Department of Infectious Diseases, İzmir, Turkey

Erdem Yaka
Dokuz Eylül University Faculty of Medicine, Department of Neurology, Division of Intensive Care, İzmir, Turkey

Özlem Öner MD, (✉),
Dokuz Eylül University Faculty of Medicine, Department of Anesthesiology and Reanimation, Division of Intensive Care, İzmir, Turkey

E-mail : namdaroner@yahoo.com
Phone : +90 232 412 12 12
ORCID ID : orcid.org/0000-0002-2836-7723

ABSTRACT *Objective:* Our aim in this study was to examine whether critically ill patients with COVID-19 achieved the targeted calories (ATC) while being treated in the intensive care unit (ICU) and their relationship with the modified Nitric score (mNUTRIC) and mortality.
Materials and Methods: Patients were divided into two groups according to whether the targeted calorie was achieved (ATC group) or not (NATC group) while staying in the ICU. Patients' mNUTRIC scores, ICU and hospital mortality rates were compared for both groups.
Results: The number of patients in the ATC group was 59 (63.4%) and the number of patients in the group that could not achieve the target calories (NATC) was 34(36.6%). mNUTRIC scores on admission were 3 (2-4) in the ATC group and 5 (4-6) in the NACT group. In multivariate regression analysis, a mNUTRIC score of 5 and higher ($p<0.01$), hemodynamic instability ($p=0.02$) and male gender ($p=0.04$) were found to be significant as independent risk factors for NATC. ICU and hospital mortality was higher in the NACT group than in the ACT group ($p<0.01$, $p<0.03$ respectively).
Conclusion: Inability to reach the targeted calories and high mNUTRIC score may be associated with mortality in critically ill COVID-19 patients treated in the ICU.
Keywords: Nutrition, targeted calory, intensive care, modified nutric score, mortality

ÖZ *Amaç:* Bu çalışmadaki amacımız, COVID-19'lu kritik hastaların yoğun bakım ünitesinde (YBÜ) tedavi edilirken hedeflenen kaloriye (ATC) ulaşıp ulaşmadığını ve bunun modifiye Nutric skoru (mNUTRIC) ve mortalite ile ilişkisini incelemekti.
Gereç ve Yöntem: Hastalar yoğun bakımda kaldıkları süre içerisinde hedeflenen kaloriye ulaşılıp ulaşılmadığına (ATC grubu) ve sağlanamamasına (NATC grubu) göre iki gruba ayrıldı. Hastaların mNUTRIC skorları, YBÜ ve hastane mortalite oranları her iki grup için karşılaştırıldı.
Bulgular: ATC grubundaki hasta sayısı 59 (%63,4), hedef kaloriye (NATC) ulaşamayan gruptaki hasta sayısı ise 34 (%36,6) idi. Başvuru anında mNUTRIC puanları ATC grubunda 3 (2-4) ve NACT grubunda 5 (4-6) olarak bulundu. Çok değişkenli regresyon analizinde mNUTRIC puanı 5 ve üzeri ($p<0.01$), hemodinamik instabilite ($p=0.02$) ve erkek cinsiyet ($p=0.04$) NATC için bağımsız risk faktörleri olarak anlamlı bulundu. YBÜ ve hastane mortalitesi NACT grubunda ACT grubuna göre daha yüksekti (sırasıyla $p<0.01$, $p<0.03$).
Sonuç: Yoğun bakım ünitesinde tedavi edilen kritik durumdaki COVID-19 hastalarında hedeflenen kaloriye ulaşamama ve yüksek mNUTRIC puanı mortalite ile ilişkilendirilebilir.
Anahtar Kelimeler: Beslenme, hedeflenen kalori, yoğun bakım, modifiye nutrik skor, mortalite

Introduction

Respiratory failure is one of the main reasons for admission of Corona virus disease (COVID-19) patients to the intensive care unit (ICU) (1). Among the COVID-19 patients which followed up ICU, the mortality rate in those treated with invasive mechanical ventilation is between 40-60% (2). SARS-CoV-2 uses the angiotensin converting enzyme 2 receptor as an entry receptor in lymphocytes, monocytes, lung alveolar type 2 cells, esophageal epithelial cells, enterocytes, and colonocytes, and produces cell damage induced by rapid viral replication, resulting in cytokine release and inflammation (3). In severe cases, increased plasma levels of proinflammatory cytokines leads to a cytokine storm (4). Cytokine storm causes damage to many organs. However, it has been reported that the priority of treatment in cytokine storm resuscitation should not cause prevention of the initiation of nutritional therapy (5).

Systemic inflammatory response and organ dysfunction in critically ill patients can lead to dysfunction in energy intake and use. In addition, it has been shown that COVID-19 patients who need invasive mechanical ventilation stay in the ICU for an average of 9 days (6). Therefore, these patients are prone to severe malnutrition and loss of muscle mass (5). Moreover, the involvement of SARS-CoV-2 in the gastrointestinal system causes negative effect on nutrition delivery, and therefore the nutritional status of COVID-19 patients; this may be one of the additional factors affecting the clinical outcome (7). There is limited information has been obtained so far about the effect of nutritional therapy in COVID-19 patients in the ICU (8). For this reason, our aim was to evaluate the nutritional risks of COVID-19 patients at admission to ICU, to determine whether appropriate nutritional goals are achieved during ICU stay, and to investigate its relationship with clinical outcomes.

Materials and Methods

This retrospective observational study was conducted in the ICU that reserved for COVID-19 patients, with the approval of the ethics committee of our University (Approval date: 18.01.2021 No:2021/02-17).

Since our study was conducted as a retrospective file review and data analysis, patient consent was waived. Between May and September 2020, COVID-19 93 patients who were confirmed by the polymerase chain reaction (PCR) test and admitted to the intensive care unit were included in the study. Those who were younger than 18 years of age, those with less than 24 hours of intensive care stay, and with insufficient medical knowledge and anamnesis were excluded from the study. Pregnant and lactating patients were also not included in the study. Demographic data, medical histories, laboratory parameters, ventilator support and mortality were retrospectively collected from the hospital records.

The disease severity of each patient within the first 24 hours after admission to the ICU was calculated according to the Acute Physiology and Chronic Health Evaluation II (APACHE II) and Sequential Organ Failure Assessment (SOFA) scoring criteria (9,10).

Nutritional risk for each patient was assessed at ICU admission using the mNUTRIC score. The score which calculated by eliminating IL-6 values, consisted of the following five variables: age, APACHE II score and SOFA score at admission, number of patients' comorbidities, and length of hospital stay before ICU (11). It has been reported that a modified NUTRIC score of 5 and above indicates that the patient has a high nutritional risk (9).

Daily needed calories and achieved values of the patients' calories, types of nutritional support (oral, enteral or parenteral) were also recorded.

In this study, the patients were divided into two groups: group of achieved the target calories (ATC) and the group that did not achieved the target calories (NACT). In order to determine on which day the target calorie (TC) was achieved if it was achieved, the amount of calories that could be given to the patient on the 1st, 2nd, 3rd, 4th, 5th, 7th, 10th and 14th days were calculated from the hospital records.

The daily calorie intake of patients was planned as 14 kcal/kg/day for patients with a body mass index (BMI) above 30 kg/m2 and 25 kcal/kg/day for patients with a body mass index below 30 kg/m2 which is as recommended by the American Society for Parenteral and Enteral Nutrition (ASPEN) and European Society for Parenteral and Enteral Nutrition (ESPEN) (12,13). The day on which the planned calories were achieved was recorded as the day on which target calory as achieved.

As hemodynamic status is an important parameter for feeding, the date of hemodynamic stabilization and the start of nutritional support were recorded. According to ICU feeding protocol systolic blood pressure of 90 mmHg and a mean arterial pressure of 65 mmHg and above without

vasopressor support or with dopamine <5 µg/kg/min or norepinephrine <0.5 µg/kg/min support was considered as hemodynamic stabilization (14). The day which the patients were hemodynamically stable and started feeding, determined and recorded. We started parenteral nutrition therapy for patients who could not tolerate enteral nutrition therapy (stopping planned feeding, gastrointestinal system (GI) intolerance (vomiting, diarrhea, bleeding) or high inotropic support).

Statistical Analysis

All continuous variables were presented as mean ± standard deviation [SD] or median (Inter-Quartile Range [IQR]) and categorical variables were presented as numbers and percentages (%). In our study we have two type of data. One of them is the categorical, the other one is numerical. We performed t-test and Mann Whitney test for numerical data otherwise we perform the Chi Square independence test for the categorical data.

Multivariate logistic regression analysis was made to investigate the risk factors for inability to reach target calorie. A p-value of<0.05 was considered statistically significant. Statistical Package for the Social Sciences (SPSS) 26.0 Statistical Package (IBM) was used for all analyses.

Results

A total of 93 confirmed COVID-19 patients were included into the study. Of the patients, 65 (69.9%) were male and 28 (30.1%) were female. Among the patients included in the study, the mean age of the ATC group was 68 (61-76), while the mean age of the NATC group was 70 (59-70) (Table 1).

Of them 59 were in ATC group and 34 were in NATC group. The median age of the patients in the (ATC) group was 68 (61-74) years, and the median age of the patients in the (NATC) group was 70 (59-77) years (p=0.89). Among the patients, APACHE II and SOFA scores were found to be significantly higher in the (NATC) group than (ATC) group (22(6-20), p=0.03; 8(6-20), p=0.02 respectively). There was

Table 1. Clinical characteristics of patient population

	All patients (n=93)	ATC group (n=59)	NACT group (n =34)	p-value
Age (year)	68 (61-76)	68 (61-74)	70 (59-77)	0.89
Gender (male)	65 (69.9)	36 (61)	29 (85.3	0.01
APACHE II score	18 (14-27)	18 (12-24)	22 (6-20)	0.03
SOFA score	8 (5.5-10.5)	6(4-8)	8 (6-10)	0.02
GCS score	14 (7.5-15)	14 (6-15)	14 (8.5-15)	0.66
BMI (kg/m^2)	27 (24-31)	27 (24-32)	28 (24-31)	0.94
Hypertension	59 (%63.4)	38 (64.4)	21 (61.8)	0.80
Diabetes mellitus	37 (39.8)	23 (39.0)	14 (41.2)	0.83
Coronary artery disease	31 (33.3)	20 (33.9)	11 (32.4)	0.88
Chronic obstructive pulmonary disease	18 (19.4)	14 (23.7)	4 (11.8)	0.16
Chronic renal failure	10 (10.8)	7 (11.9)	3 (8.8)	0.65
Congestive heart failure	14 (15.1)	10 (16.9)	4 (11.8)	0.50
Atrial fibrillation	14 (15.1)	7 (11.9)	7 (20.6)	0.26
Cirrhosis	5 (5.4)	2 (3.4)	3 (8.8)	0.26
Acute kidney failure	30 (32.3)	18 (30.5)	12 (35.3)	0.63
Cerebro-vascular event	8 (8.6)	5 (8.5)	3 (8.8)	0.95
Dementia	7 (7.5)	4 (6.8)	3 (8.8)	0.72
Parkinson's disease	2 (2.2)	1 (1.7)	1 (2.9)	0.69
Malignancy	10 (10.8)	7 (11.9)	3 (8.8)	0.65

All values are expressed as numbers (percentages) or median (interquartile range), APACHE II: Acute Physiology and Chronic Health Evaluation, SOFA: Sequential Organ Failure Assessment Score, GCS: Glasgow coma score, BMI: body mass index, SOFA score and APACHE II was calculated 24th hour ICU admission

no significant difference between the BMI of (ATC) patients and (NATC) patients (28 (24-31); p=0.94) (Table 1).

There was no significant relationship between achieve target calories (TC) and age (68(61-74), p=0.89). (Table 1).

The majority of the patients (94.6%) received nutritional treatment with the enteral nutrition (EN) method. Parenteral nutrition (TPN) was started for only 5 critically ill COVID-19 patients. In the patient group in whom parenteral nutrition was started, enteral nutrition was tried to be continued at a trophic dose. All study patients received enteral or parenteral nutrition. The feeding tube route was used in all patients who underwent enteral nutrition therapy.

The reasons that were observed for the interruption of feeding in the (NATC) group of the patients was as follows; stopping planned feeding (7, %20.6) (due to surgical procedure (2.%5.9); tracheostomy(5,%14.7)), gastrointestinal system (GI) intolerance (13, %38.2) (vomiting, diarrhea, bleeding), high inotropic support (14, %41.2). GI intolerance and high inotropic support were found to be significantly higher in the (NATC) group ((13,38.2%); (14,41.2%) respectively p=0.03 and p<0.01) (Table 3).

The mNUTRIC scores on admission to the ICU were 3(2-4) in the (ATC) group and 5(4-6) in the (NATC) group (p<0.01). In addition, as stated in the ESPEN guideline, daily 1.3 g/kg protein supplementation could be given to the ATC group, but not to the NATC group ((1, 2.9%); p<0.01) (Table-3) (12).

When the laboratory results of the patients in the (NATC) group were analyzed, it was found that the serum albumin levels on admission in the ICU the were statistically significantly lower (2.82(2.35-3.21) g/dL, p=0.03) (Table 4).

Table 2. Nutiritional charactheristics of study groups

	ATC group (n=59)	NATC group (n=34)	p-value
Target calories*	1370 (300-1500)	1370 (300-1500)	
Mean values of calories on the 1st day (min-max)	1200 (800-1400)	760 (400-1050)	<0.01
Mean values of calories on the 2nd day (min-max)	1400 (1000-1500)	1000 (800-1225)	<0.01
Mean values of calories on the 3rd day (min-max)	1400 (1000-1500)	1200 (1000-1400)	<0.01
Mean values of calories on the 4th day (min-max)	1400 (1000-1500)	1200 (980-1440)	0.07
Mean values of calories on the 5th day (min-max)	1400 (1000-1500)	1200 (980-1440)	0.07
Mean values of calories g on the 7th day (min-max)	1400 (1000-1500)	1200 (1000-1440)	0.24
Mean values of calories on the 10th DAY (min-max)	1400 (1000-1455)	1200 (970-1400)	0.15
Mean values of calories on the 14th DAY (min-max)	1100 (1000-1360)	1300 (1000-1440)	0.32
Number of days to reach target calories	2 (2-3)	-	NA

*The target calorie amount calculated according to the ESPEN and ASPEN guidelines was found to be similar in both groups

Table 3. mNUTRIC score and reasons for interruption of feeding

	ATC group (n=59)	NATC group (n=34)	p-value
mNutric score	3 (2-4)	5 (4-6)	<0.01
Additional protein intake (Number of patients-percentage)	21 (35.6%)	1 (2.9%)	<0.01
Additional vitamin intake (Number of patients-percentage)	53 (89.6)	26 (76.5)	0.05
Nutrition shutdown: planned shutdown (Number of patients-percentage)	10 (16.9%)	7 (20.6)	0.66
Suspension of feeding due to gastrointestinal intolerance (Number of patients-percentage)	11 (18.6%)	13 (38.2%)	0.03
Interruption of feeding due to hemodynamic instability (Number of patients-percentage)	9 (16.3)	14 (41.2)	<0.01

Considering both the ICU mortality rates (%88.2) and hospital mortality rates (%88.2) of COVID-19 patients followed up as critically ill in the ICU, it was found to be significantly higher in the (NATC) group (p<0.01, p<0.03 respectively) (Table 5).

When the multivariate regression analysis of risk factors related to not achieve targeted calorie was performed, mNUTRIC score of 5 and higher (OR:0.05(0.01-0.17), 95% CI; p<0.01), hemodynamic instability (p=0.02) and gender (p=0.04) were found to be significant as independent risk factors (Table 6).

Table 4. Laboratory findings on admission in the ICU

	All patients (n=59)	ATC group (n=34)	NATC group	p-value
Leukocyte 10^3/UI	11700 (9200-16000)	12800 (9700-16300)	9700 (8450-15050)	0.06
Lymphocyte 10^3/UI	500 (300-900)	500 (300-800)	550 (300-100)	0.60
Hemoglobin gr/dL	12.4 (10.8-13.4)	12.6 (10.8-13.5)	12.1 (10.4-13.3)	0.64
C-Reactive protein mg/L	146 (73-203)	141 (73-194)	161 (69-229)	0.40
Procalcitonin ng/mL	0.46 (0.11-2.19)	0.47 (011-1.53)	0.43 (0.14-3.54)	0.54
Ferritin ng/mL	476 (275-940)	461 (272-954)	620 (277-920)	0.88
Lactate dehydrogenase U/L	557 (386-728)	554 (403-684)	563 (320-761)	1.00
Alanine transaminase U/L	33 (22-64)	32 (23-65)	38 (21-60)	0.96
Aspartate aminotransferase U/L	48 (33-74)	47 (33-73)	50 (34-82)	0.51
Total bilirubin mg/dL	0.89 (0.63-1.10)	0.89 (0.62-1.11)	1.00 (0.65-1.22)	0.45
D-dimer ug/mL	1.73 (0.94-4.30)	1.50 (0.95-5.17)	1.90 (0.93-3.64)	0.67
Creatinine mg/dL	1.00 (0.76-1.80)	0.99 (0.76-1.76)	1.00 (0.79-1.85)	0.68
Albumin g/dL	3.07 (2.70-3.29)	3.07 (2.88-3.24)	2.82 (2.35-3.21)	0.03
Blood urea nitrogen mg/dL	33 (22-57)	32 (23-50)	35 (20-67)	0.65

All values are expressed as numbers (percentages) or median (interquartile range)

Table 5. Treatments and outcomes of study population

	All patients n=93	Achieved targeted calorie (n=54)	Not achieved targeted calorie (n=34)	p-value
Renal replacement therapy	26 (28%)	18 (30.5)	8 (23.5)	0.47
Tocilizumab therapy	7 (7.5%)	6 (10.2)	1 (2.9)	0.20
Intravenous corticosteroids therapy	76 (81.7)	24 (70.6)	52 (88.1)	0.127
Pulse corticosteroid therapy*	34 (34.6)	25 (42.4)	9 (26.5)	0.04
Vasopressor need**	65 (69.9)	26 (44.1)	23 (66.7)	0.03
Those who received sedation	67 (72)	43 (72.9)	24 (70.6)	0.81
Oxygen mask	25 (26.9)	16 (27.1)	9 (26.5)	1.00
High-flow nasal cannula application	26 (28%)	17 (28.8)	9 (26.5)	1.00
Non-invasive mechanical ventilator therapy	14 (15.1%)	10 (16.9)	4 (11.8)	0.56
Invasive mechanical ventilation therapy	27 (29%)	15 (25.4)	12 (35.3)	0.34
Mechanical ventilation duration (days)	5 (2-11)	4 (1-10)	2 (1-5)	0.35
Hospitalization length of stay (days)	16 (9-22)	17 (10-23)	12 (6-21)	0.04
ICU length of stay (days)	9 (4-14)	9 (5-14)	8 (3-14)	0.24
Hospital mortality rate	70 (75.3)	40 (67.8)	30 (88.2)	0.03
ICU mortality rate	68 (73.1)	38 (64.4)	30 (88.2)	0.01

All values are expressed as numbers (percentages) or median (interquartile range). *Pulse corticosteroid >250 mg/day, **Norepinephrine >30 µg/kg/min

Table 6. Multivariate regression analysis of independent risk factors for not achieved target calories group (95% CI: 95% confident interval)

	OR (95% CI)	p-value
mNutric score ≥5	0.05 (0.01-0.17)	<0.01
Hemodynamic instability	0.23 (0.06-0.82)	0.02
Gender	4.48 (1.08-18.46)	0.04
BMI	0.95 (0.85-1.06)	0.39
APACHE II score	0.95 (0.88-1.01)	0.14

Both ICU mortality rates (88.2%) and hospital mortality rates (88.2%) were higher in the NATC group (p=0.01).

Discussion

Among the 93 critically ill patients with COVID-19 treated in this study, it was found that in 59 (%) patients target calorie was achieved. mNUTRIC, APACHE II and SOFA scores in the first 24 hours were found to be significantly higher in the (NATC) group. Also in (NATC) group there was male predominancy. In the group whose TC could not be achieved, both ICU and hospital mortality were high. In the group whose targeted calorie could not be achieved, mNUTRIC score of 5 and above, hemodynamic instability and male gender were found to be significant as independent risk factors. As seen in the ICU, patients with severe forms of COVID-19 are generally aged, they have serious comorbidities, and therefore they are at risk of malnutrition and sarcopenia (15). COVID-19 patients are faced with severe respiratory tract infections and increased energy expenditure due to increased respiratory work Infection, hypermetabolism, and physical inactivity cause rapid muscle loss (16).

It was found that the general condition of the patients was poor, the critical illness scores were high, and the mortality rates were high in the group whose targeted calories could not be reached. The mNUTRIC score was also found to be high in the group that did not reach sufficient calories. Using the APACHE II score and SOFA scores when calculating the mNUTRIC score, the mNUTRIC score was high in patients with the poor general condition due to the nature of the job. It was thought that effective nutritional therapy could not be applied in this patient group due to the reasons listed.

According to a study conducted in China, 14% of COVID-19 cases were classified as severe and 5% as critically ill (17.18). In a meta-analysis investigating the mortality rate of COVID-19 patients in the ICU in China, the mortality rate was found to be 41.6%. (19). In our study, the ICU mortality of COVID-19 patients was 68%. This can be explained by the fact that patients admitted to the ICU are very severe, which is consistent with their high APACHE II, SOFA and mNUTRIC scores within the first 24 hours of admission.

In addition to affecting the lungs and inducing ARDS, coronavirus can also cause dysfunction in other organs, such as sepsis and myocardial damage (20). Patients admitted to the ICU may have a higher nutritional risk due to high viral load or excessive immune response (8). Some patients also have gastrointestinal symptoms that further increase the nutritional risk (20). In a meta-analysis of 60 studies including 4243 patients on this subject (although not all patients were critically ill), it was found that loss of appetite was seen in 26.8%, nausea-vomiting 10.2%, diarrhea 12.5%, and abdominal pain-discomfort in 9.2% (21). The development of these symptoms suggests that the severity of the disease increases (21). It has been reported that nutritional support should be started early in patients whose severity increased because intubated patients could not use the oral route during mechanical ventilation (22). Enteral nutrition (EN) should be preferred to parenteral nutrition because it is known to be associated with a lower incidence of infectious complications, fewer days of hospital stay, and reduced mortality rates as stated in previous meta-analyses (21). Although nasogastric tube application caused concern due to the risk of transmission to healthcare workers in the early stages of the pandemic, the priority of enteral nutrition was not compromised in our clinic and enteral nutrition was applied except for only 5 patients who could not tolerate enteral nutrition. It has been reported that parenteral nutrition support can be given to patients who cannot receive adequate calorie support through the enteral route (22). However, it is known that it is important to provide trophic doses of enteral nutrition for the nutrition of the intestinal mucosa, even in cases where the required calorie needs of the patients cannot be met by the enteral route (10). Thus, bacterial translocation can be prevented by

preventing atrophy of the intestinal mucosa and ensuring mucosal integrity (22, 23). In our study group, trophic dose enteral nutrition was tried in a limited number of patients with parenteral nutrition, but it was not successful.

Additionally, vasopressor therapy may increase the risk of gastrointestinal intolerance in cases of hemodynamic instability characterized by hypovolemia, hypotension, hyperlactatemia and tissue hypoperfusion (24). In this study, the presence of GIS intolerance and high-dose inotropic use was found to be statistically significant in the patient group who could not reach the target calorie. In this patient group, the same approach was generally followed and additional risk factors were evaluated. Therefore, the clinical features and nutritional status of critically ill COVID-19 patients admitted to the ICU should be analyzed in more detail. Researchers therefore drew attention to the need for nutritional risk assessment scales among adults with COVID-19 (25).

There is no gold standard for determining nutritional risk or malnutrition (24). Tools such as Mini Nutritional Assessment-Short Form, Geriatric Nutrition Risk Index, Nutritional Risk Screening 2002, Malnutrition Universal, and scoring systems such as Screening Tool, Nutritional Risk Index, Short Nutrition Assessment Questionnaire, and Nutritional Risk in Critically Patients are practical and inexpensive (25). The use of the NUTRIC scoring system in ICUs was first suggested by Canadian researchers (26). Although it is not clear which nutritional screening tool will be used in critically ill patients with COVID-19, the mNUTRIC score is a parameter that can be used in routine ICUs, including COVID-19 ICUs (11). The mNUTRIC score is user-friendly, as the variables in this scoring system are objectively obtained from the routine data in the medical records of the patients and can be easily used in patients who cannot respond verbally (11). In addition, we thought that the mNUTRIC scoring system is more useful for determining the nutritional risk of patients, since IL-6 levels are not routinely checked in our hospital.

In critically ill COVID-19 patients, Li T et al. reported a high prevalence of nutritional risk in 61% of patients in a retrospective study with data from three ICUs in Wuhan, China (17). In another study conducted in Latin America, it was found that 66% of critically ill COVID-19 patients had a high nutritional risk according to mNUTRIC-Score calculations during ICU admission (28). In our study, the group of patients whose mNUTRIC score was higher than 5 points when they were admitted to the ICU was 28%. This situation also indicates that patients with COVID-19 were at risk of malnutrition due to infection-related loss of apetite, shortness of breath, dysosmia, dysgeusia, stress, advanced age with fragility a various comorbidities, long hospital stay, isolation, and organizational problems limiting participation in meals in the period prior to their admission to the ICU (23).

Both ICU and hospital mortality rates were found higher in the NATC group. This can be explained by reasons such as increased susceptibility to infection, secondary infections, impaired immune response, higher incidence of ARDS, prolonged mechanical ventilation, acute myocardial damage, and shock (19). In addition, it is not surprising that the APACHE II and SOFA scores, which indicate the severity of critical illness, are taken as a basis when calculating the mNUTRIC score, and the mortality rates are high in those with high nutritional risk (11).

In NATC group, the decrease in serum albumin (ALB) level, which is one of the laboratory values obtained while being admitted to the ICU, was found to be statistically significant. ALB levels are the classic laboratory index in traditional nutritional assessment (29). Although not used as index of evaluation of nutritional status alone, it can provide insight into nutritional status or disease severity in clinical practice (30). Again, Wu et al. found that patients who developed ARDS had lower levels of albumin, prealbumin, and lipoprotein cholesterol.

We could not use any anthropometric measurements for nutritional assessment in this study because these data were not available in our medical records. Secondly, 93 patients who met the inclusion criteria were included and studies with larger sample sizes may be useful in this regard. Finally, randomized and controlled studies are needed because of the limitations inherent in retrospective observational studies.

Conclusion

In conclusion, nutritional support treatment can meet the patient's energy needs, prevent the negative effects of metabolism on diseases, reduce oxidative damage to cells, and regulate the immune response. Since the treatment of critical COVID-19 patients is a long process, nutritional support is an important part of the treatment and requires more attention.

As there is no gold standard for defining nutritional risk in critically ill COVID-19 patients, further development and research of disease-specific nutritional assessment tools is

needed. Therefore, the mNUTRIC score may be a suitable tool for nutritional risk assessment and prognosis prediction in critically ill COVID-19 patients.

Ethics

Ethics Committee Approval: This retrospective observational study was conducted in the ICU that reserved for COVID-19 patients, with the approval of the Ethics Committee of Dokuz Eylül University (decision no: 2021/02-17, date: 18.01.2021).

Informed Consent: Since our study was conducted as a retrospective file review and data analysis, patient consent was waived.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Ö.Ö., B.E., M.Ç.G., M.K., O.Ö.E.K., E.Y., A.N.G., Concept: Ö.Ö., B.E., M.Ç.G., M.K., O.Ö.E.K., E.Y., A.N.G., Design: Ö.Ö., B.E., M.Ç.G., M.K., O.Ö.E.K., E.Y., A.N.G., Data Collection and Process: Ö.Ö., B.E., M.Ç.G., M.K., O.Ö.E.K., E.Y., A.N.G., Analysis or Interpretation: Literature Search: Ö.Ö., B.E., M.Ç.G., M.K., O.Ö.E.K., E.Y., A.N.G., Writing: Ö.Ö., B.E., M.Ç.G., M.K., O.Ö.E.K., E.Y., A.N.G.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Rodriguez-Morales AJ, Cardona-Ospina JA, Gutiérrez-Ocampo E, Villamizar-Peña R, Holguin-Rivera Y, Escalera-Antezana JP, et al. Clinical, laboratory and imaging features of COVID-19: A systematic review and meta-analysis. Travel Med Infect Dis. 2020;34:101623.
2. Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. Lancet Respir Med. 2020;8(5):475-81.
3. Hellewell J, Abbott S, Gimma A, Bosse NI, Jarvis CI, Russell TW, et al. Feasibility of controlling COVID-19 outbreaks by isolation of cases and contacts. Lancet Glob Health. 2020;8(4):e488-e96.
4. Armitage R, Nellums LB. COVID-19 and the consequences of isolating the elderly. Lancet Public Health. 2020;5(5):e256.
5. Li XY, Du B, Wang YS, Kang HYJ, Wang F, Sun B, et al. [The keypoints in treatment of the critical coronavirus disease 2019 patient(2)]. Zhonghua Jie He He Hu Xi Za Zhi. 2020;43(4):277-81.
6. Grasselli G, Zangrillo A, Zanella A, Antonelli M, Cabrini L, Castelli A, et al. Baseline Characteristics and Outcomes of 1591 Patients Infected With SARS-CoV-2 Admitted to ICUs of the Lombardy Region, Italy. Jama. 2020;323(16):1574-81.
7. Thibault R, Seguin P, Tamion F, Pichard C, Singer P. Nutrition of the COVID-19 patient in the intensive care unit (ICU): a practical guidance. Crit Care. 2020;24(1):447.
8. Li G, Zhou CL, Ba YM, Wang YM, Song B, Cheng XB, et al. Nutritional risk and therapy for severe and critical COVID-19 patients: A multicenter retrospective observational study. Clin Nutr. 2021;40(4):2154-61.
9. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. Crit Care Med. 1985;13(10):818-29.
10. Vincent JL, Moreno R, Takala J, Willatts S, De Mendonça A, Bruining H, et al. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. On behalf of the Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine. Intensive Care Med. 1996;22(7):707-10.
11. Zhang P, He Z, Yu G, Peng D, Feng Y, Ling J, et al. The modified NUTRIC score can be used for nutritional risk assessment as well as prognosis prediction in critically ill COVID-19 patients. Clin Nutr. 2021;40(2):534-41.
12. Singer P, Blaser AR, Berger MM, Alhazzani W, Calder PC, Casaer MP, et al. ESPEN guideline on clinical nutrition in the intensive care unit. Clin Nutr. 2019;38(1):48-79.
13. Mechanick JI, Carbone S, Dickerson RN, Hernandez BJD, Hurt RT, Irving SY, et al. Clinical Nutrition Research and the COVID-19 Pandemic: A Scoping Review of the ASPEN COVID-19 Task Force on Nutrition Research. JPEN J Parenter Enteral Nutr. 2021;45(1):13-31.
14. Zheng YY, Ma YT, Zhang JY, Xie X. COVID-19 and the cardiovascular system. Nat Rev Cardiol. 2020;17(5):259-60
15. Rice TW,Wheler AP, Thompson BT,et al. Initial trophic vs full enteral feeding in patients with acute lung injury, the EDEN randomized trial. JAMA. 2012;307(8):795-803
16. Chen T, Wu D, Chen H, Yan W, Yang D, Chen G, et al. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. Bmj. 2020;368:m1091.
17. Li T, Zhang Y, Gong C, Wang J, Liu B, Shi L, et al. Prevalence of malnutrition and analysis of related factors in elderly patients with COVID-19 in Wuhan, China. Eur J Clin Nutr. 2020;74(6):871-5.
18. Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention. Jama. 2020;323(13):1239-42.
19. Armstrong R, Kane A, Cook T. Outcomes from intensive care in patients with COVID-19: a systematic review and meta-analysis of observational studies. Anaesthesia. 2020;75(10):1340-9.
20. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020;395(10229):1054-62.
21. Gu J, Han B, Wang J. COVID-19: Gastrointestinal Manifestations and Potential Fecal-Oral Transmission. Gastroenterology. 2020;158(6):1518-9.
21. Cheung KS, Hung IFN, Chan PPY, Lung KC, Tso E, Liu R, et al. Gastrointestinal Manifestations of SARS-CoV-2 Infection and Virus Load in Fecal Samples From a Hong Kong Cohort: Systematic Review and Meta-analysis. Gastroenterology. 2020;159(1):81-95.
22. Farina N, Nordbeck S, Montgomery M, Cordwin L, Blair F, Cherry-Bukowiec J, et al. Early Enteral Nutrition in Mechanically Ventilated Patients With COVID-19 Infection. Nutr Clin Pract. 2021;36(2):440-8.
23. Martindale R, Patel JJ, Taylor B, Arabi YM, Warren M, McClave SA. Nutrition Therapy in Critically Ill Patients With Coronavirus Disease 2019. JPEN J Parenter Enteral Nutr. 2020;44(7):1174-84.
24. Reignier J, Boisramé-Helms J, Brisard L, Lascarrou JB, Ait Hssain A, Anguel N, et al. Enteral versus parenteral early nutrition in ventilated adults with shock: a randomised, controlled, multicentre, open-label, parallel-group study (NUTRIREA-2). Lancet. 2018;391(10116):133-43.
25. Silva DFO, Lima S, Sena-Evangelista KCM, Marchioni DM, Cobucci RN, Andrade FB. Nutritional Risk Screening Tools for Older Adults with COVID-19: A Systematic Review. Nutrients. 2020;12(10).
26. Rahman A, Hasan RM, Agarwala R, Martin C, Day AG, Heyland DK. Identifying critically-ill patients who will benefit most from nutritional therapy: Further validation of the "modified NUTRIC" nutritional risk assessment tool. Clin Nutr. 2016;35(1):158-62.
27. Liu G, Zhang S, Mao Z, Wang W, Hu H. Clinical significance of nutritional risk screening for older adult patients with COVID-19. Eur J Clin Nutr. 2020;74(6):876-83.
28. Osuna-Padilla IA, Rodríguez-Moguel NC, Aguilar-Vargas A, Rodríguez-Llamazares S. High nutritional risk using NUTRIC-Score is associated with worse outcomes in COVID-19 critically ill patients. Nutr Hosp. 2021.
29. Beck FK, Rosenthal TC. Prealbumin: a marker for nutritional evaluation. Am Fam Physician. 2002;65(8):1575-8.
30. Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, et al. Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China. JAMA Intern Med. 2020;180(7):934-43.