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Original article

mNUTRIC tool is capable to predict nutritional needs and mortality early in patients suffering from severe pneumonia



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SUMMARY

Objective: This retrospective observational study aims to evaluate the prognostic accuracy of Modified Nutrition Risk in Critically ill (mNUTRIC) compared to Nutrition Risk Score-2002 (NRS-2002) in patients hospitalized in the intensive care unit due to severe pneumonia during the pandemic period.

Methods: RT-PCR test and Chest CT was performed in all patients in the emergency department pandemic area. The CURB-65 at the time of admission to the emergency department and Acute Physiology and Chronic Health Evaluation II (APACHE II), Sequential organ failure assessment score (SOFA), NRS-2002 and mNUTRIC scores 24 h after hospitalization in the intensive care unit were calculated. The analysis of the data was made in IBM SPSS Statistics Base 22.0 package program.

Results: One hundred and twenty-five patients found to have severe pneumonia based on the chest CT taken in the emergency department pandemic area and hospitalized in the intensive care unit were included in the study. A real-time reverse transcription PCR (RT-PCR) test was positive in 30.4% (n: 38) of the patients. Additional nutrition treatment was initiated in 54.4% of the patients. In the analytical evaluation to predict nutritional treatment needs, mNUTRIC's AUC value (AUC: 0.681, 95% 0.582–0.780, $p < 0.001$) was higher than NRS-2002. While 64.8% (n: 81) of the patients were discharged, 35.2% (n: 44) died. In the analytical evaluation to predict mortality, the AUC value of mNUTRIC had the highest value (AUC: 0.875, 95% CI 0.814–0.935, $p < 0.001$).

Conclusion: The mNUTRIC score can predict at an early period the nutritional needs and mortality of patients with severe pneumonia during the Covid-19 pandemic.

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1. Introduction

Malnutrition, impaired wound healing in patients with critical disease, and high nosocomial infection rates are associated with one another and are strong indicators of morbidity and mortality due to all causes [1]. The nutritional status of patients admitted to the ICU is also affected by the severity of the underlying pathophysiological processes that cause hospitalization rather than

chronic or acute starvation [1]. Researches indicate that patients infected with Coronavirus disease (COVID-19) in 2019 suffered from fever, cough, shortness of breath, muscle pain, confusion, headache, sore throat, chest pain, respiratory failure, diarrhea, nausea and vomiting, loss of taste and smell senses [2]. All of these complaints can disrupt nutritional status as they interfere with immune function, food intake and absorption. Therefore, early screening of nutritional status in patients with SARS-COV-2 infection also helps to control malnutrition.

Proper screening and evaluation of nutritional status is very important in intensive care patients. This screening not only identifies malnutrition in patients who may benefit from nutritional intervention, but also can predict morbidity and mortality at an early time [3]. The European Society of Parenteral and Enteral

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Nutrition (ESPEN) recommends the use of Nutritional Risk Score 2002 (NRS-2002) [4] and the American Society for Enteral and Parenteral Nutrition (ASPEN) [5] recommends NRS-2002 and the NUTRIC scores for critically ill patients. NRS-2002 [6] is the first screening tool developed to evaluate nutritional status. NRS-2002 is effective in identifying patients with nutritional risk who can benefit from early and aggressive nutritional support [7,8]. It can be applied to all hospitalized patients, but it is not a specially developed score for intensive care patients. NUTRIC score [9] is the first nutritional risk tool developed to define the nutritional risk in intensive care patients who can benefit from aggressive nutrition therapy [10]. ASPEN guidelines recommend classified patients as “under risk of malnutrition” if NRS 2002 ≥ 3 and as “at high risk of malnutrition” if NRS-2002 is ≥ 5 and modified NUTRIC (mNUTRIC) is ≥ 5 [5]. Screening the nutritional status of patients with suspected and confirmed Covid-19 pneumonia and detecting the patients with high risk early can help provide timely nutritional support and predict mortality.

This study aims to compare the prognostic accuracy of mNUTRIC calculated in patients hospitalized in the intensive care unit with the diagnosis of severe pneumonia during the Covid-19 pandemic with NRS-2002.

2. Materials and method

This retrospective observational study was initiated after obtaining the approval of the Republic of Turkey Ministry of Health (2020-05-30T14 07 42.xml) and the local ethics committee (Approval Date: 03/06/2020, Decision Number: 914/58). Patients who had severe pneumonia that was coherent with COVID 19 in the thorax computed tomography (CT) performed in the pandemic area of the tertiary hospital emergency department between 20/03/2020 and 25/05/2020 and hospitalized in the intensive care unit were included in the study. The admission criteria for severe pneumonia were according to guidelines published by the Turkey Ministry of Health for management of patients with suspected COVID-19 pneumonia and included a combination of clinical, laboratory and radiologic information [11].

Patients with pneumonia coherent with Covid-19 in chest CT were grouped as mild, moderate, severe pneumonia according to their clinical and laboratory findings. Patients with severe pneumonia and hospitalized for at least 24 h in the intensive care unit were included in the study. Severe pneumonia was defined as patients with 1) respiratory distress with a respiratory rate over 30 breaths per minute, (2) oxygen saturation $\leq 93\%$ in the resting state, (3) arterial blood oxygen partial pressure (PaO₂)/oxygen concentration (FiO₂) ≤ 300 mm Hg, 4) requiring mechanical ventilation or non-invasive mechanical ventilator 5) in shock and/or requiring hemodynamic support and/or requiring vasopressor. Excluding criteria of the study 1) hospitalized in the ICU for less than 24 h 2) pregnant 3) incomplete data 4) patients under 18.

Demographic features, vital signs, additional diseases, laboratory parameters, Chest CT finding, Covid-19 RT-PCR test results, duration of hospitalization, patients' need for mechanical ventilator, vasopressor and renal replacement therapy, nutritional needs, nutritional therapies and outcome data were obtained from patient files and hospital electronic data processing system records.

2.1. Study variables

The CURB-65 score, which is one of the pneumonia severity scores and includes five risk factors (confusion or decreased consciousness, blood urea nitrogen >7 mmol/L, respiratory frequency 30/min, systolic blood pressure <90 mmHg or diastolic blood pressure 60 mmHg, and age 65 years) was calculated from the file

data recorded during the application of the patients to the emergency department and recorded in the data collection form.

The APACHE II score (history of severe organ failure, age, body temperature, mean arterial blood pressure, heart rate, respiratory rate, Ph, inspired fraction of oxygen (FiO₂), arterial oxygen tension (A-aPO₂) or arterial oxygen pressure (PaO₂), arterial pH or HCO₃, serum sodium and potassium, creatinine serum levels, acute renal failure, hematocrit, leukocytes, and Glasgow coma score), which is one of the intensive care severity scores and SOFA score (Partial O₂ pressure, FiO₂, on mechanical ventilation, Platelets, Glasgow coma scale, Bilirubin, Mean arterial pressure or Administration of vasoactive agents required, Serum creatinine levels) were calculated 24 h after hospitalization in the intensive care and recorded in the hospital electronic data system.

Body mass index (BMI) is defined as a person's weight in kilograms divided by the square of the person's height in metres (kg/m²). It is calculated by the nutrition team and recorded in the hospital electronic data system. Patients were categorized as underweight (BMI ≤ 18.5), normal weight (BMI 18.5–24.9), overweight (BMI 25–29.9) and obese (BMI ≥ 30) [12].

We used the NRS 2002 and mNUTRIC as a nutritional screening tool. NRS 2002 and mNUTRIC scores were calculated by the nutrition team 24 h after hospitalization in the intensive care unit and recorded in the hospital electronic data system. The NRS-2002 is the nutritional screening tool recommended by ESPEN [4]. NRS-2002 was applied the way it was recommended in the literature. Since all the patients were severe intensive care patients, the second stage of questions in which BMI, weight loss and food intake were analyzed was started. In the second stage, the questions of nutritional impairment, severity of disease and age (≥ 70 age) were completed and the patient was classified over a total of 7 points. If NRS-2002 was <3 , there was no nutritional risk; if NRS 2002 was ≥ 3 , there was under nutritional risk; and if NRS 2002 was ≥ 5 , there was high nutritional risk [5] and the classifications were made based on this. mNUTRIC score (without IL-6) includes criteria for age, APACHE II score, SOFA score, comorbidities, and days in hospital to ICU admission. The total score is 9. Patients with mNUTRIC ≥ 5 were defined as having high risk [5].

Statistical Analysis: Average, standard deviation, median lowest, highest, frequency and ratio values were used in the descriptive statistics of the data. The distribution of variables was measured using the Kolmogorov–Smirnov test. Independent sample t-test and Mann–Whitney U and One Way Anova test were used in the analysis of quantitative independent data. In the analysis of qualitative independent data, Chi-square test was used and when the Chi-square test conditions were not met, Fisher's exact test was used. The power of NRS-2002 and mNUTRIC scores to predict nutritional treatment needs was measured by ROC analysis. Sensitivity and specificity were calculated by finding a cut-off point that would have a high diagnostic accuracy for the scores. The power of CURB-65, SOFA, APACHE II, NRS-2002 and mNUTRIC scores to predict mortality was measured by ROC analysis. Sensitivity and specificity were calculated by finding a cut-off point that would have a high diagnostic accuracy for the scores. SPSS 22.0 program was used in the analyses. p value was considered significant when it was under 0.05.

3. Results

A total of 125 suspected and confirmed Covid-19 severe pneumonia patients, including 64% (n: 80) males and 36% (n: 45) females, were included in the study (Table 1). 75.2% (n: 94) of the patients in the study were over 65 years old and the mean age was 69.2 ± 14.4 years. The mean of BMI was 26.6 ± 6.8 kg/m². Statistically significant BMI was found in patients with a mortal course

Table 1
Demographics and clinical presentation in patients with suspected and confirmed Covid-19 severe pneumonia.

	Total 125 (100%)	Survivor 81 (64.8%)	Non Survivor 44 (35.2%)	p
Gender				
Female	45 (36%)	28 (34.6%)	17 (38.6%)	0.699
Male	80 (64%)	53 (65.4%)	27 (61.4%)	
Age (years) (mean ± SD)	69.2 ± 14.4	68.4 ± 15.2	70.7 ± 12.9	0.407
Age Group n (%)				
<65 years	31 (24.8%)	21 (25.6%)	10 (23.3%)	0.830
≥65 years	94 (75.2%)	61 (74.4%)	33 (76.7%)	
BMI (mean ± SD)	26.6 ± 6.8	25.5 ± 5.3	28.6 ± 8.3	0.034
BMI Group n (%)				
<18.5 kg/m ² (n %)	15 (12%)	5 (6.2%)	10 (22.7%)	0.010
18.5–24.9 kg/m ²	47 (37.6%)	45 (55.6%)	2 (4.5%)	<0.001
25–29.9 kg/m ²	29 (23.2%)	16 (19.8%)	13 (29.5%)	0.268
≥30 kg/m ²	34 (27.2%)	15 (18.5%)	19 (43.2%)	0.006
Fever (°C)	37.4 ± 0.9	37.4 ± 0.9	37.5 ± 0.9	0.456
Pulse (beats/min)	110.4 ± 22.0	108.5 ± 21.9	113.9 ± 22.4	0.200
MAP (mmHg)	81.8 ± 28.1	87.4 ± 30.1	71.4 ± 20.6	<0.001
Respiratory Rate (beats/min)	33.2 ± 3.3	32.2 ± 3.3	35.0 ± 2.4	0.247
Saturation (%)	88.6 ± 4.7	87.9 ± 5.7	88.9 ± 3.9	0.247
HT	79 (63.2%)	54 (66.7%)	25 (56.8%)	0.333
DM	43 (34.4%)	30 (37%)	13 (29.5%)	0.436
CAD	43 (34.4%)	29 (35.8%)	14 (31.8%)	0.697
COPD	34 (27.2%)	24 (29.6%)	10 (22.7%)	0.528
CVD	26 (20.8%)	21 (25.9%)	5 (11.4%)	0.067
CKD	24 (19.2%)	16 (19.8%)	8 (18.2%)	1.000
Cancer	21 (16.8%)	9 (11.1%)	12 (27.3%)	0.026
Suspicious contact	57 (45.6%)	43 (53%)	14 (31.8%)	0.025
Fever	54 (43.2%)	35 (43.2%)	19 (43.2%)	1.000
Dry cough	82 (65.6%)	49 (60.5%)	33 (75%)	0.118
Dyspnea	92 (73.6%)	54 (66.7%)	38 (86.4%)	0.020
Chest pain	7 (5.6%)	5 (6.2%)	2 (4.5%)	1.000
Abdominal pain	28 (22.4%)	19 (23.5%)	9 (20.5%)	0.719
Nausea -Vomiting	62 (49.6%)	40 (49.4%)	22 (50%)	1.000
Positive RT-PCR test	38 (30.4%)	25 (30.9%)	13 (29.5%)	1.000
Symptoms onset to the first visit, (day)	3.5 ± 2.1	3.1 ± 1.9	4.2 ± 2.2	0.009
GGO	76 (60.8%)	47 (58%)	29 (65.9%)	0.446
Consolidation	23 (18.4%)	15 (18.5%)	8 (18.2%)	1.000
GGO + Consolidation	46 (36.8%)	27 (33.3%)	19 (43.2%)	0.333
LDH (5–247 U/L)	478.3 ± 566.7	487.4 ± 678.2	495.00 ± 786.264	0.760
Urea (mg/dl)	91.1 ± 59.1	89.2 ± 59.5	94.7 ± 58.9	0.622
Creatinine (0.51–0.95 mg/dl)	2.9 ± 3.1	3.1 ± 3.4	2.5 ± 2.4	0.245
Ferritin (11–307 µg/L)	651.4 ± 921.7	698.8 ± 1003.5	564 ± 751.2	0.437
WBC (3.8–11.8103/µl)	10.8 ± 5.9	10.3 ± 5.0	11.7 ± 7.3	0.217
Neutrophils (1.9–8.2103/µl)	8.4 ± 5.2	7.8 ± 4.2	9.5 ± 6.5	0.074
Lymphocytes (1.1–3.1103/µl)	1.5 ± 1.8	1.6 ± 1.9	1.3 ± 1.7	0.292
NLR	10.3 ± 13.1	8.4 ± 7.5	13.9 ± 19.3	0.024
Fibrinogen (180–350 mg/dl)	478.5 ± 209.3	486.7 ± 210.3	463.4 ± 209.1	0.555
D-Dimer (0–630 µg/L)	5493.1 ± 13212.2	3402.1 ± 4592.6	9342.5 ± 20994.1	0.016
Hs-Tn I (0–16 ng/L)	419.9 ± 1597.2	330.8 ± 1356.9	583.8 ± 1972	0.451
CRP (0–5 mg/L)	116.5 ± 104.5	101.1 ± 102.6	144.8 ± 103.1	0.025
Albumin (35–55 g/L)	30.1 ± 6.2	31.6 ± 6	27.4 ± 5.6	<0.001

SD; Standard Deviation BMI; Body Mass Index, BMI: <18.5 kg/m² underweight, 18.5–24.9 kg/m² normal weight, 25–29.9 kg/m² overweight, ≥ 30 kg/m² obese MAP: Mean arterial pressure HT: Hypertension, DM: Diabetes Mellitus, CAD: Coronary Artery Disease, COPD: Chronic Obstructive Pulmonary Disease, CVD: Cerebrovascular Disease CKD; Chronic Kidney Disease, RT-PCR; Real-time polymerase chain reaction, GGO; Ground glass opacity, LDH; Lactate dehydrogenase, WBC; White blood cell, NLR; Neutrophil/Lymphocytes ratio, hs-Tn I; High sensitivity troponin I, CRP; C-reactive protein.

($p = 0.034$). While the BMI of 37.6% ($n = 47$) of our patients was in the normal weight (18.5–24.9) category, the mortality rate in this category was 4.3% ($n = 2$). Mortality was statistically significant in patients with BMI ≤18.5 (underweight) and BMI ≥ 30 (obese) categories ($p = 0.010$ $p = 0.006$, respectively) (Table 1). At least one comorbid disease was present in 94.4% ($n = 118$) of the patients. Hypertension, diabetes, and coronary artery disease (CAD) were the most common (63.2%, 34.4% and 34.4% respectively). Patients were admitted to the emergency department mostly with the complaints of shortness of breath, dry cough and gastrointestinal symptoms (73.6%, 65.6% and 52.8%, respectively).

The average time that the patients admitted to the emergency department after the onset of symptoms was 3.5 ± 2.1 days. It was determined that this period was statistically significant with

mortality ($p = 0.009$, Table 1) and need for nutritional therapy ($p < 0.001$). When the relationship between the onset of symptoms and emergency admission and the need for nutritional therapy was examined, it was seen that it was 2.7 ± 1.7 days on average in survivor patients and 4.2 ± 2.1 days on average in non-survivor patients ($p < 0.001$).

RT-PCR test and Chest CT was performed in all patients in the emergency department pandemic area. Chest CT of all patients also had findings suggesting pneumonia, while RT-PCR test was positive in 30.4% ($n = 38$). Ground glass opacity was the most commonly observed finding 60.8% ($n = 76$) of the patients' Chest CT (Table 1). CT images of PCR (+) and PCR (–) patients are presented in Fig. 1.

The average number of hospitalization days of the patients was 17.2 ± 14.6 . While 64.8% ($n = 81$) of the patients were discharged,

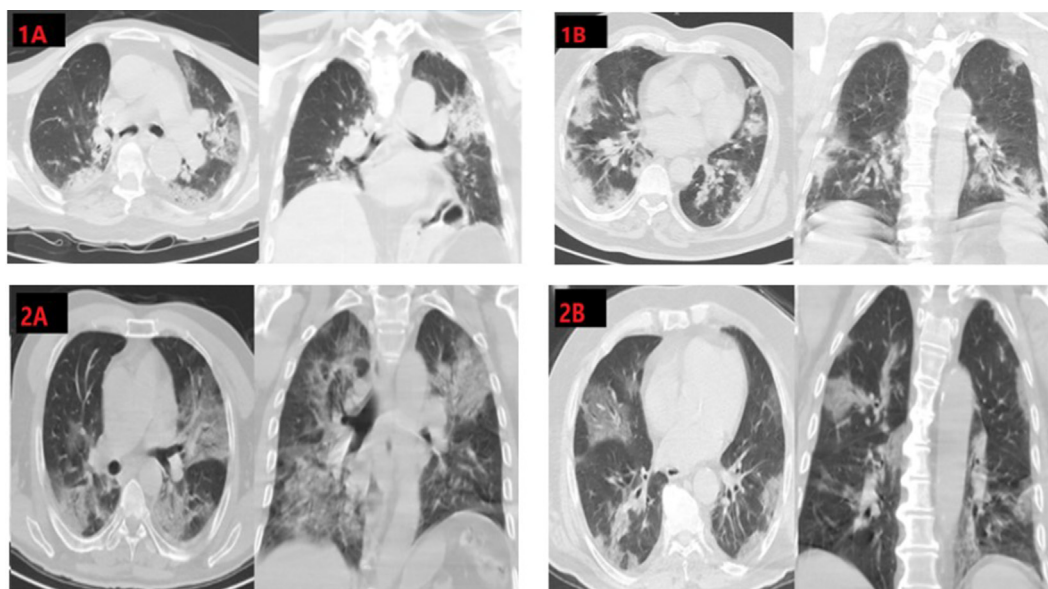


Fig. 1. Features of demographic and Chest CT findings of RT-PCR positive and negative patients. 1A: 69 years old, non-survivor male patient, RT-PCR test was negative, Chest CT: multifocal peripheral consolidations in the left lung upper lobe and both lung lower lobes and focal ground glass opacities (GGO) appearance in the left lung upper lobe were observed. 1B: 74 years old, survivor, male patient, RT-PCR test was negative, her wife's RT-PCR test was positive, Chest CT: Widespread sub pleural GGO and consolidation areas are observed in both lungs. 2A: 62 years old, non-survivor, male patient, RT-PCT test was positive, Chest CT: In the lung parenchyma areas, there are common patch-style GGO and consolidated areas in the periphery. 2B: 80 years old, non-survivor, male patient, RT-PCR test was positive, Chest CT: Diffuse GGO containing air bronchograms were observed in both lungs.

35.2% (n: 44) died. Demographic data and vital parameters of survivor and non-survivor patients are presented in Table 1.

When the relationship between scores and mortality is examined, mNUTRIC score was 4 ± 1.6 on average in survivor patients, it was 6.4 ± 1.2 on average in non-survivor patients ($p < 0.001$). The other scores are presented in the Table 2.

When the scores for nutritional risk assessment are examined, according to NRS-2002, 86.4% (n: 108) of patients were found to be at risk of malnutrition ($NRS-2002 \geq 3$), and 30.4% (n: 38) at high risk of malnutrition ($NRS-2002 \geq 5$). No mortality was detected in patients with $NRS 2002 < 3$, but 21 patients with $NRS 2002 \geq 5$ died, which was statistically significant. ($p = 0.004$) (Table 2). According to the mNUTRIC score, 56.8% (n: 71) were found to be under high risk of malnutrition ($mNUTRIC \geq 5$). 41 patients with $mNUTRIC \geq 5$ died, which was statistically significant ($p < 0.001$). 54.4% (n: 68) of the patients were provided with additional nutritional support for 2.5 ± 1.6 days on average. In the study, 82.3% of the patients who received normal oral nutrition ($p < 0.001$) and 86.6% of the patients who received oral nutrition therapy survived ($p = 0.004$). Enteral and parenteral nutrition therapy data are presented in Table 2.

Predictive power of NRS-2002 and mNUTRIC across Gender, Age and BMI categories were examined. No statistically significant correlation was found between gender and NRS 2002 ($p = 0.407$) and mNUTRIC ($p = 0.060$). The mNUTRIC score was found to be statistically significantly higher in patients over 65 years of age ($p < 0.001$). There was no statistical difference between BMI categories and NRS 2002 ($p = 0.833$). mNUTRIC score was statistically significantly higher in patients with BMI < 18.5 and ≥ 30 ($p < 0.001$) (Table 3).

The graphic of the ROC analysis performed to determine the nutritional requirement predictive characteristics of mNUTRIC and NRS-2002 in the whole patient group is presented in Fig. 2. In the analytical evaluation performed to determine nutritional treatment needs; while mNUTRIC's AUC was 0.681, 95% 0.582–0.780, $p < 0.001$, NRS-2002's AUC was 0.624, 95% CI 0.524–0.725, $p < 0.001$ (Table 4).

Table 2

Comparison of ICU treatments and scores of survivor and non-survivor severe pneumonia patients.

	Total 125 (100%)	Survivor 81 (64.8%)	Non Survivor 44 (35.2%)	p
Antibiotic	121 (96.8%)	77 (95.1%)	44 (100%)	0.296
Praqueniil	119 (100%)	77 (95.1%)	42 (95.5%)	1.000
Oseltamivir	101 (80.8%)	62 (76.5%)	39 (88.6%)	0.153
Favipiravir	35 (28%)	19 (23.5%)	16 (36.4%)	0.147
Oxapar (LMWH)	84 (67.2%)	51 (63%)	33 (75%)	0.231
Normal oral feeding	85 (68%)	70 (86.4%)	15 (34.1%)	<0.001
Nutritional therapy	68 (54.4%)	37 (45.7%)	31 (70.5%)	0.009
-Enteral Nutrition	62 (49.6%)	32 (39.5%)	29 (66%)	0.007
NG Tube	42 (33.6%)	15 (18.5%)	27 (61.4%)	<0.001
Oral	30 (24%)	26 (32.1%)	4 (9.1%)	0.004
-Parenteral Nutrition	26 (20.8%)	15 (18.5%)	11 (25%)	0.489
Nutrition start time (day)	2.5 ± 1.6	2.8 ± 1.5	2.1 ± 1.5	0.502
NIMV	63 (50.4%)	51 (63%)	12 (27.3%)	<0.001
MV Requirement	72 (57.6%)	32 (39.5%)	40 (91%)	<0.001
RRT	39 (31.2%)	25 (30.9%)	14 (31.8%)	1.000
Vasopressor Requirement	86 (68.8%)	45 (55.6%)	41 (93.2%)	<0.001
SOFA	6.5 ± 3.1	5.6 ± 3	8.1 ± 2.8	<0.001
APACHE II	17.7 ± 7.7	15.9 ± 7.5	21 ± 7	<0.001
CURB-65	3.8 ± 1	3.5 ± 1	4.3 ± 0.7	<0.001
mNUTRIC (mean \pm SD)	4.9 ± 1.9	4 ± 1.6	6.4 ± 1.2	<0.001
mNUTRIC Group n (%)				
<5	54 (43.2%)	51 (63%)	3 (6.8%)	<0.001
≥ 5	71 (56.8%)	30 (37%)	41 (93.2%)	<0.001
NRS-2002 (Mean \pm SD)	3.8 ± 1	3.5 ± 1.1	4.4 ± 0.7	<0.001
NRS-2002 Group n (%)				
<3	17 (13.6%)	17 (21%)	0 (0%)	0.001
3 -4	70 (56%)	47 (58%)	13 (52.3%)	0.575
≥ 5	38 (30.4%)	17 (21%)	21 (47.7%)	0.004
Length of Hospital Stay	17.2 ± 14.6	17.2 ± 12.9	17.3 ± 17.4	0.987

SD: Standard Deviation, LMWH; Low-molecular-weight heparin, SOFA Score: Sequential organ failure assessment score, APACHE II: Acute Physiology and Chronic Health Evaluation II, CURB-65: Confusion, Urea, Respiratory Rate, Blood Pressure and Age ≥ 65 , mNUTRIC: Modified Nutrition Risk in Critically ill score, NRS-2002: Nutritional Risk Screening-2002, MV: Mechanical Ventilator, RRT: Renal Replacement Therapy, NIMV; Non-Invasive Mechanical Ventilator, NRS 2002 < 3; No risk of malnutrition, NRS 2002 $\geq 3 - <5$; under risk of malnutrition, NRS-2002 ≥ 5 ; high risk of malnutrition, mNUTRIC ≥ 5 ; high risk of malnutrition.

Table 3
Power of prediction of NRS-2002 and mNUTRIC score across Gender, Age and BMI categories.

	NRS-2002	p	mNUTRIC	p
Gender				
Female	3.9 ± 1.01	0.407	5.3 ± 1.6	0.060
Male	3.8 ± 1.04		4.7 ± 2	
Age (years)				
<65 years	3.5 ± 0.8	0.071	3.7 ± 1.9	<0.001
≥65 years	3.9 ± 1.1		5.3 ± 1.7	
BMI				
<18.5 kg/m ²	4.3 ± 0.6	0.833	6.1 ± 1.7	<0.001
18.5–24.9 kg/m ²	3.5 ± 1.1		4.2 ± 1.7	
25–29.9 kg/m ²	3.6 ± 1.0		4.7 ± 1.7	
≥30 kg/m ²	4.2 ± 0.9		5.5 ± 1.8	

BMI; Body Mass Index, BMI: <18.5 kg/m² underweight, 18.5–24.9 kg/m² normal weight.

25–29.9 kg/m² overweight, ≥ 30 kg/m² obese; NRS-2002: Nutritional Risk Screening-2002.

mNUTRIC: Modified Nutrition Risk in Critically ill score.

In the analytical evaluation performed to determine MV Requirement, while mNUTRIC's AUC was 0.855, 95% 0.786–0.924, $p < 0.001$, NRS-2002's AUC was 0.803, 95% CI 0.721–0.885, $p < 0.001$. In the analytical evaluation performed to determine Vasopressor Requirement, while mNUTRIC's AUC was 0.861, 95% 0.792–0.929, $p < 0.001$, NRS-2002's AUC was 0.743, 95% CI 0.647–0.839, $p < 0.001$. In the analytical evaluation performed to determine the RRT, noninvasive and duration of hospital stay between nutrition scores, it revealed no statistically significant relationship between them.

The graphic of ROC analysis performed to determine the mortality predictive characteristics of CURB-65, SOFA, APACHE II, mNUTRIC and NRS-2002 in the whole patient group has been presented in Fig. 3. When the ROC analysis performed to determine the mortality predictive characteristics of the scores was examined, it was determined that the AUC value of the mNUTRIC (AUC: 0.875, 95% CI 0.814–0.935, $p < 0.001$) was the highest. The other scores are presented in the Table 5.

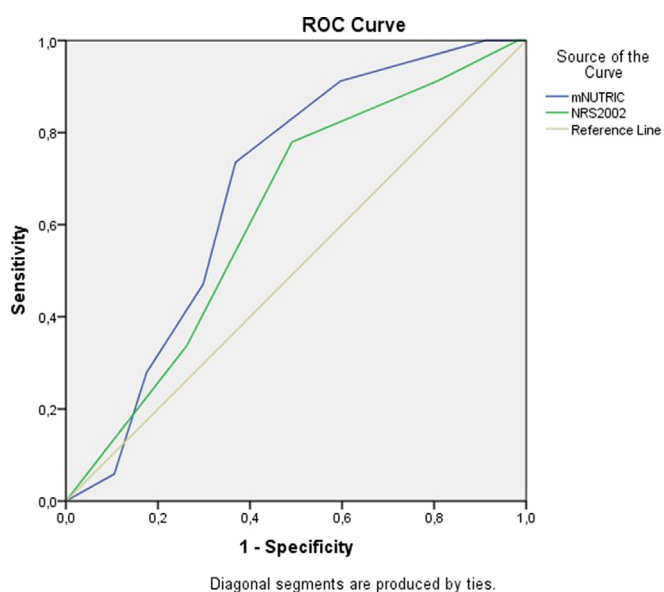


Fig. 2. The graphic of the ROC analysis performed to determine the nutritional requirement predictive characteristics of mNUTRIC and NRS-2002 in the whole patient group.

4. Discussion

The objective of this study is to compare the prognostic accuracy of the mNUTRIC score, one of the nutritional risk tool for critically ill patients used to discriminate who's nutritionally high risk and therefore would benefit more from nutritional therapy, with NRS 2002. In the analytical evaluation, for nutritional treatment need, mNUTRIC's AUC was 0.681, 95% 0.582–0.780, $p < 0.001$, while for mortality mNUTRIC's AUC was 0.875, 95% CI 0.814–0.935, $p < 0.001$. As a result of our data, we found out that mNUTRIC score also predicted mortality while determining the nutritional requirement in the early period in patients who were hospitalized in the ICU due to severe pneumonia. As a result of our data, we found that the mNUTRIC score predicts mortality while determining the nutritional need in the early period in patients hospitalized in the intensive care unit due to severe pneumonia.

Recent evidence examining adults infected with COVID-19 shows that malnutrition has a significant impact on health outcomes. Multiple comorbidities, advanced age and malnutrition increase the risk of death in COVID-19 infections. There is important evidence indicating that protein-energy malnutrition resulting from inadequate dietary intake may increase the risk of infectious disease [13]. Therefore, nutritional care to identify and handle malnutrition is also critical in the treatment and prevention of adverse health consequences following COVID-19 infection. The incidence of malnutrition is higher in elderly patients with COVID-19. First, the protein that forms the muscles is consumed by the acute inflammatory response of Covid-19 infection. Inflammation indicators of patients (ferritin, tumor necrosis factor alpha, interleukin family factors, etc.) increase [14]. The synthesis of these acute phase proteins leads to the consumption of albumin and muscle proteins [14]. Second, SARS-CoV-2 can attack mucosal epithelium and therefore might cause gastrointestinal symptoms that further disrupt patients' nutritional status [15]. Gastrointestinal symptoms (diarrhea, mild abdominal pain, nausea, vomiting, loss of appetite) caused by SARS-CoV-2 may exacerbate malnutrition in elderly patients [15]. It is reported that approximately 40% of patients with critical disease besides COVID-19 infection develop acute renal failure (ARF) [16]. Although the exact cause of ARF in these patients is unknown, it is thought that the dehydration that starts before application contributes to such a failure. While 61.6% (n: 77) of our patients had gastrointestinal symptoms at the time of application, 52.8% (n: 66) of them had acute renal failure. Late admission to the ICU increases the mortality rate in CAP [17]. In our study, the time of admission to the emergency service after the onset of symptoms was statistically significantly longer in both patients with additional nutritional needs and non-survivor patients. This situation affected the nutritional status of our patients with severe pneumonia, and further aggravated their existing clinics.

Many scoring systems are used to recognize the risk factors affecting mortality in patients with pneumonia in intensive care and to evaluate the severity of the disease. The use of scoring systems enables decision-making as regards the treatment site and assessment of the risk of mortality for community-acquired pneumonia patients (CAP). CURB-65 Score is a pneumonia severity score [18] developed to decide whether for outpatient treatment or for inpatient treatment for CAP and studies have shown that it can also be used to predict mortality [19]. In recent studies, it was found that the CURB-65 score was significantly higher in COVID-19 patients who died [20]. In a recently published work by Zhou et al., higher SOFA score was found to be associated with mortality [20]. Zhang et al. found that high APACHE II and SOFA scores were associated with an increased risk of death in their study on patients with Covid-19 infection [21]. In our study, the

Table 4
ROC Analysis of the Nutritional needs prediction of mNUTRIC and NRS-2002.

	AUC	SE	% 95 CI	Cut-off	Sensitivity	Specificity	p
mNUTRIC	0.681	0.051	0.582–0.780	4.5	73.5	63.2	<0.001
NRS-2002	0.624	0.051	0.524–0.725	3.5	77.9	50.9	0.017

AUC: Areas under the curve, SE: Standard Error, CI: Confidence Interval, mNUTRIC: Modified Nutrition Risk in Critically ill score, NRS-2002: Nutritional Risk Screening-2002.

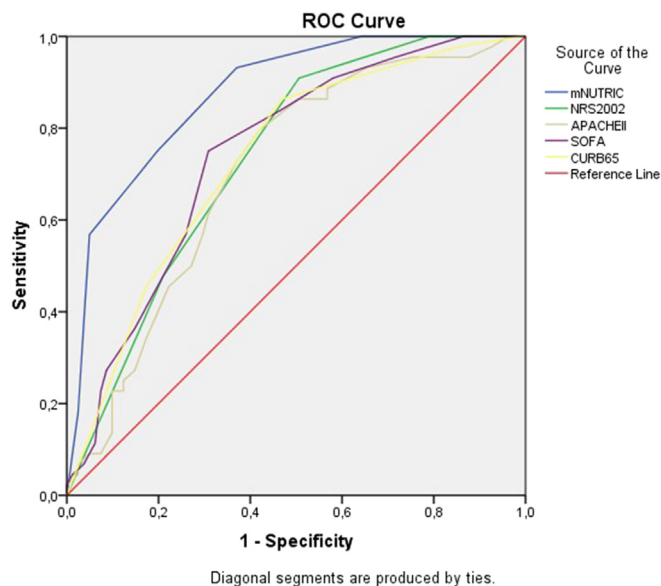


Fig. 3. The graphic of ROC analysis performed to determine the mortality predictive characteristics of CURB-65, SOFA, APACHE II, mNUTRIC and NRS-2002 in the whole patient group.

disease severity scores (CURB-65, SOFA, APACHE II) of all patients hospitalized due to severe pneumonia were high, and statistically significantly higher in mortal patients ($p < 0.001$, $p < 0.01$ and $p < 0.01$, respectively).

In recent studies, advanced age and male gender have been identified as risk factors for serious illness and death in COVID-19 patients [20,22–24]. While increasing age and gender were not found to be statistically significant in terms of mortality in our study, more extensive studies are needed to evaluate this result.

Acknowledging that BMI is also likely an important determinant of outcome, a recent analysis by Heyland et al. demonstrated that an increase of 1000 cal per day was associated with an overall reduction in mortality (odds ratio for 60-day mortality 0.76, 95% confidence intervals (CI), 0.61–0.95, $p = 0.014$) [25]. Surprisingly, the improved mortality effect from increased calories was specifically seen in patients whose body mass index (BMI) was below 25 or above 35. For patients with BMIs between 25 and 35, no benefit was seen [25]. As a result of our analysis, the mortality rate was

Table 5
mNUTRIC, NRS-2002, SOFA, APACHE II and CURB-65 of ROC Analysis of Mortality Prediction.

	AUC	SE	% 95 CI	Cut-off	Sensitivity	Specificity	p
mNUTRIC	0.875	0.031	0.814–0.935	4.5	93.2	63	<0.001
SOFA	0.745	0.044	0.659–0.832	5.5	84.1	53.1	<0.001
NRS-2002	0.736	0.044	0.651–0.822	3.5	90.9	49.4	<0.001
CURB-65	0.733	0.046	0.644–0.823	3.5	86.4	53.1	<0.001
APACHE II	0.706	0.047	0.614–0.798	15.5	79.5	58	<0.001

AUC: Areas under the curve, SE: Standard Error, CI: Confidence Interval, CURB-65: Confusion, Urea, Respiratory Rate, Blood Pressure and Age ≥ 65 , SOFA Score: Sequential organ failure assessment score, mNUTRIC: Modified Nutrition Risk in Critically ill score, APACHE II: Acute Physiology and Chronic Health Evaluation, NRS-2002: Nutritional Risk Screening-2002.

statistically significantly higher in patients hospitalized due to severe pneumonia with BMI ≤ 18.5 (underweight) and BMI ≥ 30 (obese). The mNUTRIC score was found to be statistically significantly higher in patients with BMI ≤ 18.5 (underweight) and BMI ≥ 30 (obese) and older age (≥ 65 years). The mNUTRIC score can help patients with features such as older age, underweight or obese hospitalized in the intensive care unit in terms of appropriate treatment. Coupled with idea that critical illness itself affects nutrition risk by means of starvation and inflammation, the concept that ICU patients respond differently to nutrition therapy led to the development of several tools to assess the nutritional risk of individual ICU patients. We think that larger studies should be carried out, emphasizing the importance of applying a special tool that screens mortality and nutrition in critically ill patients, taking into account age and BMI.

In studies performed on ICU patients, high NRS-2002 score has been shown to have a positive relationship with mortality as well as with risk of malnutrition [6]. Various studies in the intensive care unit related to the mNUTRIC score have shown a significant relationship between mNUTRIC score and mortality [26,27]. In also a study on patients with Covid-19 infection, mNUTRIC was found to be associated with mortality [28]. In our study, we found that the power of mNUTRIC score to predict mortality risk in suspected and confirmed Covid-19 pneumonia patients hospitalized in the intensive care was statistically significant (AUC: 0.875, $p < 0.001$) and higher than NRS-2002 (AUC:0.736, $p < 0.001$). In our study, it was observed that mNUTRIC score, a nutritional screening tool developed specifically for intensive care patients, could also predict mortality just as other severity scores (CURB-65, SOFA, APACHE II) could predict in patients with severe pneumonia; however, it could at the same time determine the need for early nutrition.

The mNUTRIC score evaluated together with the APACHE II and SOFA scores, which determine the severity of the disease, does not contain any nutritional parameters such as NRS-2002 [9]. It is known that mNUTRIC ≥ 5 in intensive care patients predicts high nutritional risk, aggressive nutritional needs and mortality [29]. Kalaiselvan et al. [30] found that 43% of patients were at high risk of malnutrition in a study they performed in patients on mechanical ventilators and Mendes et al. [26] found that 49% were under risk of malnutrition (mNUTRIC ≥ 5). Zhang et al. [28] found this rate as 61% in a study conducted in patients with Covid-19. In our study, in the evaluation made through nutritional risk tools, 56.8% (n: 71) of patients were found to be under high risk of malnutrition according to mNUTRIC score (mNUTRIC ≥ 5). Additional nutritional supportive

therapy was initiated in 54.4% of the patients. When nutritional tools were analyzed in our study, the mNUTRIC score was found to be statistically significant in predicting nutritional needs in patients hospitalized in intensive care unit due to suspected and confirmed covid-19 severe pneumonia and it was higher than NRS-2002.

Critical intensive care patients should be provided with small frequent feeds, including high energy and protein foods and oral nutritional supplements. If protein and energy needs cannot be met by oral intake, nutritional support should be initiated. In adults who require nutritional support in the intensive care unit, enteral nutrition (EN) should be provided if the patient is hemodynamically stable and there is no gastrointestinal (GI) dysfunction [31,32]. Although EN is typically the preferred route of nutritional support, airway complications may occur in patients with non-invasive mechanical ventilator (NIMV), and therefore parenteral nutrition (PN) may be considered under these conditions [30]. Nutritional support should be initiated as soon as possible, ideally within 36 h after hospitalization or 12 h after intubation [32]. In our study, three types of nutritional support were provided to the patients by the nutrition team. Patients were fed primarily with normal oral feeding (hospital meal) (68%). As a result of nutritional risk assessment through nutritional risk tools, additional nutritional support (54.4%) including enteral (49.6%) (Oral, NG) and parenteral (20.8%) support was provided to patients at high risk or who had malnutrition within an average of 2.5 ± 1.6 days. It is known that poor nutritional status is associated with mortality [26]. In also our study, a statistically significant relationship was found between poor nutritional status and mortality ($p = 0.009$). Of the surviving patients, 86.4% ($n = 70$) were fed through normal oral feeding, and 32.1% ($n = 26$) through oral nutrition therapy. Mortality was statistically low in both groups fed orally ($p < 0.001$, $p = 0.004$, respectively). Additional nutritional support in the early stages of the current ICU treatment and, if possible, to provide oral feeding may contribute to the reduction of mortality rates.

The fact that our study was single-centered and retrospective and could only be conducted regarding severe patients and the fact that there was a small number of patients may pose a limitation. There is no comparison to other ICU populations, for example, liver cirrhosis, brain tumor etc. The study focuses on baseline assessment of NRS-2002 and mNUTRIC, whereas further evaluation in the course of ICU treatment is not available. The primary outcome analysis is restricted to mean 17-day mortalities, whereas ICU mortality is not taken into account. No follow-up after discharge is considered. Moreover, this study has no interventional design. The effects and adequacy of nutritional therapy on the outcome or length of ICU stay were not assessed. This limitation reemphasizes the need for prospective studies based on NUTRIC or mNUTRIC. It may be useful to carry out future studies on nutritional evaluation in patients with pneumonia in a wider universe.

5. Conclusion

Nutritional risk tools should be used in the early period in patients hospitalized in intensive care because of severe pneumonia during the Covid pandemic period. Providing early and effective enteral nutritional support as part of intensive care therapy in intensive care patients can contribute to patient outcomes. Although the mNUTRIC score is limited in its ability to detect malnutrition, it can benefit the clinician by helping to categorize ICU patients and guide the clinician towards appropriate treatment. However; it is important to recognize that not all ICU patients will respond the same to nutritional interventions, and that was the main concept behind the NUTRIC score, as most other risk scores and assessment tools consider all critically ill patients to be at high nutrition risk.

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Ethics approval

This study started after obtaining ethics approval from the Republic of Turkey Ministry of Health then T. C. Adana City Training and Research Hospital, Hospital Scientific Research Evaluation Commission (Date of Approval: 03/06/2020 Decision Number: 914 Number: 58).

Authors' contributions

SA, MG, SS, NU, CI, HES and EG conceived and designed the study; SA, MG, HES, CI and EG selected the articles and extracted the data; SA, MG, NU, HES and EG analyzed the data and interpreted the results; SA, MG, NU, HES, CI, EG and SS contributed to writing the final version of the manuscript. All authors agreed with the results and conclusions of this article.

Declaration of competing interest

The authors declare no conflicts of interest.

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References

- [1] Omar M, Elfagi S, Nough F. Covid-19 and nutrition: review of available evidence. *Sch J App Med Sci*. 2020. <https://doi.org/10.36347/sjams.2020.v08i04.025>. ISSN 2347–954X (Print)/ISSN 2320-6691.
- [2] Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* 2020;395:507–13.
- [3] Budzyński J, Tojek K, Czerniak B, Banaszkiewicz Z. Scores of nutritional risk and parameters of nutritional status assessment as predictors of in-hospital mortality and readmissions in the general hospital population. *Clin Nutr* 2016;35(6):1464–71. <https://doi.org/10.1016/j.clnu.2016.03.025>.
- [4] Kondrup J, Allison SP, Elia M, Vellas B, Plauth M. Educational and clinical practice committee, European society of parenteral and enteral nutrition (ESPEN). Educational and clinical practice committee, European society of parenteral and enteral nutrition (ESPEN). ESPEN guidelines for nutrition screening. *Clin Nutr* 2003;22:415–21.
- [5] McClave SA, Taylor BE, Martindale RG, Warren MM, Johnson DR, Braunschweig C, McCarthy MS, Davanos E, Rice TW, Cresci GA, Gervasio JM, Sacks GS, Roberts PR, Compher C. Society of critical care medicine; American society for parenteral and enteral nutrition. Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient: society of critical care medicine (SCCM) and American society for parenteral and enteral nutrition (A.S.P.E.N.). *JPEN - J Parenter Enter Nutr* 2016;40(2):159–211.
- [6] Marchetti J, Dos Reis AM, Dos Santos AF, Luft VC, Steemburgo T. High nutritional risk is associated with unfavorable outcomes in patients admitted to an intensive care unit. *Rev Bras Ter Intensiva* 2019;31(3):326–32.
- [7] Johansen N, Kondrup J, Plum LM, Bak L, Nørregaard P, Bunch E, et al. Effect of nutritional support on clinical outcome in patients at nutritional risk. *Clin Nutr* 2004;23(4):539–50.
- [8] Starke J, Schneider H, Alteheld B, Stehle P, Meier R. Short-term individual nutritional care as part of routine clinical setting improves outcome and quality of life in malnourished medical patients. *Clin Nutr* 2011;30(2):194–201.
- [9] Heyland DK, Dhaliwal R, Jiang X, Day AG. Identifying critically ill patients who benefit the most from nutrition therapy: the development and initial validation of a novel risk assessment tool. *Crit Care* 2011;15(6):R268.
- [10] Rosa M, Heyland DK, Fernandes D, Rabito EI, Oliveira ML, Marcadenti A. Translation and adaptation of the NUTRIC Score to identify critically ill patients who benefit the most from nutrition therapy. *Clin Nutr ESPEN* 2016;14:31e6. <https://doi.org/10.1016/j.clnesp.2016.04.030>.

- [11] Turkish Ministry of Health. COVID-19 (SARS-CoV-2 infection) guideline, 14 April 2020. Ankara: Turkish Ministry of Health; 2020.
- [12] BMI classification. Global database on body mass index. World Health Organization; 2006. Retrieved. . [Accessed 27 July 2012].
- [13] Farhadi S, Ovchinnikov RS. The relationship between nutrition and infectious diseases: a review. *Biomed Biotechnol Res J* 2018;2:168–72.
- [14] Jia H. Pulmonary angiotensin-converting enzyme 2 (ACE2) and inflammatory lung disease. *Shock* 2016;46:239–48.
- [15] Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020;395(10223):497–506. [https://doi.org/10.1016/S0140-6736\(20\)30183-5](https://doi.org/10.1016/S0140-6736(20)30183-5).
- [16] Cheng Y, Luo R, Wang K, Zhang M, Wang Z, Dong L, et al. Kidney disease is associated with in-hospital death of patients with COVID-19. *Kidney Int* 2020;97(5):829–38.
- [17] Marti C, Garin N, Grosgrain O, Poncet A, Combescurie C, Carballo S, et al. Prediction of severe community acquired pneumonia: a systematic review and meta-analysis. *Crit Care* 2012;16:141.
- [18] Charles PG, Davis JS, Grayson ML. Rocket science and the infectious diseases society of America/American thoracic society (IDSA/ATS) guidelines for severe community-acquired pneumonia. *Clin Infect Dis* 2009;48(12):1796–7. <https://doi.org/10.1086/599227>.
- [19] Zhang ZX, Yong Y, Tan WC, Shen L, Ng HS, Fong KY. Prognostic factors for mortality due to pneumonia among adults from different age groups in Singapore and mortality predictions based on PSI and CURB-65. *Singap Med J* 2018;59(4):190–8. <https://doi.org/10.11622/smedj.2017079>.
- [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] Zhang G, Hu C, Luo L, Fang F, Chen Y, Li J, et al. Clinical features and short-term outcomes of 221 patients with COVID-19 in Wuhan, China. *J Clin Virol* 2020;104364. <https://doi.org/10.1016/j.jcv.2020.104364>.
- [22] Du RH, Liang LR, Yang CQ, Wang W, Cao TZ, Li M, et al. Predictors of mortality for patients with COVID-19 pneumonia caused by SARS-CoV-2: a prospective cohort study. *Eur Respir J* 2020 Jan:1.
- [23] Zhang J, Wang X, Jia X, Li J, Hu K, Chen G, et al. Risk factors for disease severity, unimprovement, and mortality of COVID-19 patients in Wuhan, China. *Clin Microbiol Infect* 2020 Apr 15;26(6):767–72. <https://doi.org/10.1016/j.cmi.2020.04.012>.
- [24] Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW, et al. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area. *J Am Med Assoc* 2020 Apr 22;26(323(20)):2052–9. <https://doi.org/10.1001/jama.2020.6775>.
- [25] Alberda C, Gramlich L, Jones N, Jeejeebhoy K, Day AG, Dhaliwal R, et al. The relationship between nutritional intake and clinical outcomes in critically ill patients: results of an international multicenter observational study. *Intensive Care Med* 2009;35:1728–37. <https://doi.org/10.1007/s00134-009-1567-4>.
- [26] Mendes R, Policarpo S, Fortuna P, Alves M, Virella D, Heyland DK. Nutritional risk assessment and cultural validation of the modified NUTRIC score in critically ill patients-A multicenter prospective cohort study. *J Crit Care* 2017;37:45e9.
- [27] Mukhopadhyay A, Henry J, Ong V, Leong JSF, Teh AL, van Dam RM, et al. Association of modified NUTRIC score with 28-day mortality in critically ill patients. *Clin Nutr* 2017;36:1143–8.
- [28] Zhang P, Zhigang H, Yu G, et al. The modified NUTRIC score can be used for nutritional risk assessment as well as prognosis prediction in critically ill COVID-19 patients *Clinical Nutrition* 2020;7:10.
- [29] Maciel LRMA, Franzosi OS, Nunes DSL, Loss SH, Reis AMD, Rubin BA, et al. Nutritional risk screening 2002 cut-off to identify high-risk is a good predictor of ICU mortality in critically ill patients. *Nutr Clin Pract* 2019;34(1):137–41. <https://doi.org/10.1002/ncp.10185>.
- [30] Kalaiselvan MS, Renuka MK, Arunkumar AS. Use of nutrition risk in critically ill (NUTRIC) score to assess nutritional risk in mechanically ventilated patients: a prospective observational study. *Indian J Crit Care Med* 2017;21(5):253e6.
- [31] Barazzoni R, Bischoff SC, Breda J, Wickramasinghe K, Krznaric Z, Nitzan D, et al. ESPEN expert statements and practical guidance for nutritional management of individuals with SARS-CoV-2 infection. *Clin Nutr* 2020;39(6):1631–8. <https://doi.org/10.1016/j.clnu.2020.03.022>.
- [32] American Society for Parenteral and Enteral Nutrition. Nutrition therapy in the patient with COVID-19 disease requiring ICU care. 2020. <https://www.nutritioncare.org/%20uploaded%20Files/%20Documents/%20Guidelines%20and%20Clinical%20Resources/%20Nutrition%20Therapy%20COVID-19%20SCCM-ASPEN.pdf>.