

# Comparison of NRS-2002 and mNUTRIC scores to assess nutritional risk and predict medical intensive care unit mortality: A prospective observational study

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## Abstract

**Aim:** The intensive care unit (ICU) treats patients with diverse diagnoses, yet no gold-standard tool exists to assess nutritional risk and predict mortality. The American Society for Parenteral and Enteral Nutrition (ASPEN) recommend the use of the Nutritional Risk Screening-2002 (NRS-2002) and the modified Nutrition Risk in the Critically Ill score (mNUTRIC). This study aimed to determine nutritional risk using these tools and compare their performance in predicting ICU mortality.

**Methods:** This prospective observational study included 201 patients aged  $\geq 18$  years treated in the Medical ICU of Adana City Training and Research Hospital between April and October 2022. Patients were classified as survivors or non-survivors and followed until discharge or death. Nutritional risk was assessed using NRS-2002 and mNUTRIC, and their predictive performance for mortality was evaluated using receiver operating characteristic (ROC) analysis.

**Results:** Among 201 patients (57.7% male, mean age  $63.06 \pm 17.52$  years), nutritional risk was identified in 81.6% by NRS-2002 and 25.9% by mNUTRIC. The ICU mortality rate was 45.8% (n=92). Non-survivors had significantly higher median NRS-2002 [4.5 (2-7)] and mNUTRIC [5 (1-9)] scores compared to survivors (p<0.001). The area under the ROC curve (AUC) for predicting mortality was 0.792 (95% CI: 0.732-0.849) for NRS-2002 and 0.851 (95% CI: 0.796-0.901) for mNUTRIC (p<0.05). Optimal cutoff values were  $>4$  for NRS-2002 and  $>5$  for mNUTRIC.

**Conclusion:** Both NRS-2002 and mNUTRIC identified patients at nutritional risk and predicted ICU mortality. The mNUTRIC score demonstrated superior predictive accuracy. Cutoff values of  $\geq 4$  for NRS-2002 and  $\geq 5$  for mNUTRIC may serve as useful predictors of ICU mortality.

**Keywords:** Intensive care unit; nutritional status; NRS-2002; mNUTRIC score

## 1. Introduction

The prevalence of malnutrition among intensive care unit (ICU) patients ranges from 38% to 78%.<sup>1</sup> As malnutrition is associated with higher complication rates, prolonged hospital stays, increased mortality, and greater healthcare costs, it represents a major risk factor in critical care.<sup>2</sup> Early identification and individualized nutritional support have been shown to reduce length of stay, infectious complications, and overall healthcare expenditure, thereby improving clinical outcomes.<sup>3</sup> Consequently, nutritional screening is essential for identifying critically ill patients at risk of malnutrition.<sup>1</sup> However, no evidence-based screening tool with high sensitivity and specificity has been universally accepted for detecting malnutrition or predicting nutritional risk in critically ill populations.<sup>4</sup>

According to the 2019 European Society for Clinical Nutrition and Metabolism (ESPEN) guideline, all patients staying in the ICU for longer than 48 hours are considered at risk of malnutrition.<sup>5</sup> The American Society for Parenteral and Enteral Nutrition (ASPEN) rec-

ommend nutritional screening within the first 48 hours of ICU admission using either the Nutritional Risk Screening-2002 (NRS-2002) or the modified Nutrition Risk in the Critically Ill score (mNUTRIC).<sup>6</sup> NRS-2002 is one of the most widely used nutritional screening tools worldwide<sup>7</sup> and has been mandated in Türkiye since 2018 by the Ministry of Health for the assessment of all hospitalized patients.<sup>8</sup> Developed by Kondrup et al.<sup>9</sup>, the tool evaluates nutritional status and disease severity, with a total score  $\geq 3$  indicating malnutrition risk. Nonetheless, its use in ICUs may be limited by challenges in obtaining accurate body weight in critically ill patients, as weight can be affected by edema, plasmapheresis, and fluid therapy.<sup>5</sup>

Given the close link between malnutrition and inflammation in critical illness, screening tools incorporating inflammatory markers have been needed.<sup>2</sup> The Nutrition Risk in the Critically Ill (NUTRIC) score was developed by Heyland et al. to address this gap.<sup>10</sup> Because interleukin-6 (IL-6) is not routinely measured in clinical practice

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and the score performs similarly without it, Rahman et al. proposed the mNUTRIC score.<sup>11</sup> High mNUTRIC scores (>5) have been associated with increased mortality and inadequate nutritional intake.<sup>11</sup> A large prospective observational study also demonstrated a significant positive correlation between increasing mNUTRIC scores and mortality among both surgical and medical ICU patients.<sup>12</sup> Similarly, another study reported that mNUTRIC is a suitable tool for assessing nutritional risk and prognosis in neurological ICU patients.<sup>13</sup> A single-center retrospective study from Turkey found malnutrition risk in one-third of critically ill COVID-19 pneumonia patients and identified high mNUTRIC scores as a predictor of increased mortality.<sup>14</sup>

Assessing nutritional risk in critically ill patients remains challenging due to the heterogeneity and limitations of existing screening tools. Nevertheless, early identification of malnutrition followed by individualized nutrition therapy has the potential to reduce mortality. Existing studies have generally focused on patient groups with uniform clinical diagnoses. Therefore, the aim of the present study was to determine nutritional risk using NRS-2002 and mNUTRIC in a heterogeneous medical ICU population and to compare the ability of these tools to predict ICU mortality.

## 2. Materials and Methods

### *Ethical and Research Approvals*

Ethical approval for this prospective observational study was obtained from the Clinical Research Ethics Committee of the Adana City Training and Research Hospital, (approval date: 11.03.2019, decision number: 602). Due to the COVID-19 pandemic, additional approval was obtained to extend the study period until 31.03.2021, after which the study commenced. All procedures were carried out in accordance with institutional and national ethical standards and with the principles of the Declaration of Helsinki, revised in 2013. Informed consent was obtained from all participants or their first-degree relatives.

### *Setting and Sample*

All adult patients ( $\geq 18$  years) treated in the ICU of Adana City Training and Research Hospital between April 2022, and October 2022 were included. Exclusion criteria were pregnancy or lactation, age <18 years, refusal of written informed consent by the patient or a first-degree relative, ICU stay <24 hours, and death within the first 24 hours. During the six-month inclusion period, all eligible patients were consecutively enrolled without sampling. A total of 201 patients meeting the criteria were classified as survivors or non-survivors and were followed until discharge or death.

### *Data collection*

The Acute Physiology and Chronic Health Evaluation II (APACHE II) and Sequential Organ Failure Assessment (SOFA) scores were calculated and recorded by the attending intensivist within the first 24 hours of ICU admission. The APACHE II score consists of acute physiology, age, and chronic health components, with a maximum score of 71.<sup>15</sup> The SOFA score evaluate six organ systems (respiratory, coagulation, hepatic, cardiovascular, renal, and central nervous system) and ranges from 0 (best) to 24 (worst) points.<sup>16</sup>

Patient demographics (age, sex), primary ICU admission diagnosis, length of ICU stay, and need for mechanical ventilation were retrieved from electronic medical records. Information on weight loss in the preceding three months and reduced oral intake during the previous week was obtained from patients and/or their caregivers.

### *Evaluation of nutritional status and Anthropometric measurements*

Nutritional risk assessments were performed by a dietitian within the first 48 hours of ICU admission using the NRS-2002 and

the mNUTRIC scores. In this study, patients with NRS-2002  $\geq 3$  or mNUTRIC >5 were classified as high nutritional risk, whereas those with NRS-2002 <3 and mNUTRIC <5 were considered not at risk. All patients received individualized nutrition support based on age, sex, and physiological status. Disease severity was categorized as none, mild, moderate, or severe according to NRS-2002 criteria.<sup>9</sup>

Height and body weight were measured by nursing staff when feasible; if direct measurement was not possible, patient or caregiver reports were used. Body mass index (BMI) was calculated as weight (kg) divided by height<sup>2</sup> (m<sup>2</sup>).<sup>17</sup>

### *Statistical analysis*

Descriptive statistics for categorical variables were presented as frequencies and percentages, and comparisons were conducted using the Pearson chi-square test. The Shapiro-Wilk test was used to assess the normality of numerical variables. Numerical data were reported as mean  $\pm$  standard deviation for normally distributed variables and as median (min-max) for non-normally distributed variables. Independent group comparisons for non-normally distributed variables were performed using the Mann-Whitney U test.

Correlations between numerical variables were analyzed using Spearman's rank correlation coefficient, with interpretations based on the following criteria: <0.2 very weak, 0.2-0.4 weak, 0.4-0.6 moderate, 0.6-0.8 strong, and >0.8 very strong correlation.<sup>18</sup> Receiver operating characteristic (ROC) analysis was applied to evaluate overall discriminatory power and determine optimal cutoff values. Statistical significance was set at  $p < 0.05$ ,  $p < 0.01$ , and  $p < 0.001$  (two-tailed). All analyses were performed using SPSS v27 (IBM Inc., Chicago, IL, USA).

## 3. Results

Among the 201 patients included in the study, 116 were male (57.7%) and 85 were female (42.3%), with a mean age of  $63.06 \pm 17.52$  years. The most common reason for ICU admission was cancer (23.4%), followed by other diagnoses (22.9%), chronic kidney failure (19.9%), gastrointestinal diseases (13.9%), diabetes (7.5%), and sepsis (2%). Overall, 11.4% of the patients required mechanical ventilation, 37.8% had mild disease severity, 62.2% reported weight loss in the past three months, and 82.6% had reduced oral intake during the previous week. Nutritional risk was identified in 81.6% of patients according to NRS-2002 and in 25.9% according to mNUTRIC (Table 1, Table 2).

Patients were categorized as survivors or non-survivors. The mortality rate was 45.8%, with males comprising 60.9% of the non-survivor group. Cancer was the leading admission diagnosis among non-survivors (31.5%), 82.6% had comorbidities, and 18.5% required mechanical ventilation. Based on nutritional screening, 98.9% of non-survivors were at risk according to NRS-2002 and 46.7% according to mNUTRIC, whereas 67% of survivors were at risk according to NRS-2002 and 8.3% according to mNUTRIC.

Significant differences were observed between survivors and non-survivors in terms of age, length of ICU stay, APACHE II score, SOFA score, number of comorbidities, NRS-2002 score, and mNUTRIC score ( $p < 0.01$ ;  $p < 0.001$ ). Non-survivors had higher median values for age [70.5 (19-91) vs. 64 (18-91)], ICU stay duration [7 (2-51) vs. 3 (2-17)], APACHE II score [22.5 (1-46) vs. 10 (0-43)], SOFA score [5.5 (0-14) vs. 3 (0-10)], and number of comorbidities [3 (0-6) vs. 2 (0-5)] compared with survivors ( $p < 0.01$ ;  $p < 0.001$ ) (Table 2).

Regarding nutritional risk, non-survivors had significantly higher NRS-2002 scores [4.5 (2-7)] than survivors [3 (0-6)], and higher mNUTRIC scores [5 (1-9)] than survivors [3 (0-8)] ( $p < 0.001$ ) (Table 2).

**Table 1**

Descriptive statistics of demographic, anthropometric, and health findings according to patients' mortality status

Mortality Status	Yes (n=92)		No (n=109)		Total (n=201)		$\chi^2$	p
	n	%	n	%	n	%		
<b>Gender</b>								
Male	56	60,9	60	55,0	116	57,7	$\chi^2=0,693$	0,405
Female	36	39,1	49	45,0	85	42,3		
<b>Type of Diagnosis*</b>								
Chronic kidney failure	23	25,0	17	15,6	40	19,9	$\chi^2=15,760$	0,015*
Diabetes	6	6,5	9	8,3	15	7,5		
Cardiovascular disease	4	4,3	17	15,6	21	10,4		
Gastrointestinal system diseases	9	9,8	19	17,4	28	13,9		
Cancer	29	31,5	18	16,5	47	23,4		
Sepsis	2	2,2	2	1,8	4	2,0		
Other	19	20,7	27	24,8	46	22,9		
<b>Presence of Comorbidities</b>								
Yes	76	82,6	68	62,4	144	71,6	$\chi^2=10,043$	0,002**
No	16	17,4	41	37,6	57	28,4		
<b>Mechanical Ventilation Status</b>								
No	75	81,5	103	94,5	178	88,6	$\chi^2=8,287$	0,004**
Yes	17	18,5	6	5,5	23	11,4		
<b>Severity Level of Illness</b>								
None	0	0,0	5	4,6	5	2,5	$\chi^2=68,863$	<0,001***
Mild	9	9,8	67	61,5	76	37,8		
Moderate	41	44,6	25	22,9	66	32,8		
Severe	42	45,7	12	11,0	54	26,9		
<b>Three-Month Weight Loss Status</b>								
Yes	76	82,6	49	45,0	125	62,2	$\chi^2=30,083$	<0,001***
No	16	17,4	60	55,0	76	37,8		
<b>Reduced Food Intake Status</b>								
Yes	84	91,3	82	75,2	166	82,6	$\chi^2=8,965$	0,003**
No	8	8,7	27	24,8	35	17,4		
<b>NRS-2002 Risk Status</b>								
No nutritional risk (<3)	1	1,1	36	33,0	37	18,4	$\chi^2=33,888$	<0,001***
Nutritional risk ( $\geq 3$ )	91	98,9	73	67,0	164	81,6		
<b>mNUTRIC Risk Status</b>								
No nutritional risk ( $\leq 5$ )	49	53,3	100	91,7	149	74,1	$\chi^2=38,525$	<0,001***
Nutritional risk (>5)	43	46,7	9	8,3	52	25,9		

mNUTRIC, modified nutritional risk score for critically ill patients; NRS-2002, nutritional risk screening-2002

**Table 2**

Descriptive statistics of age, anthropometric measurement value, APACHE-II, SOFA, NRS-2022 and mNUTRIC scores according to individuals' mortality status

	Mortality Status							U	p
	Yes		No		Total				
	$\bar{X} \pm SS$	Median (min-max)	$\bar{X} \pm SS$	Median (min-max)	$\bar{X} \pm SS$	Median (min-max)			
Age (years)	67,25±15,40	70,5 (19-91)	59,52±18,47	64 (18-91)	63,06±17,52	67 (18-91)	3747,5	0,002**	
Body Weight (kg)	71,92±14,39	70,5 (40-140)	73,24±15,92	75 (40-120)	72,64±15,21	73 (40-140)	4767,5	0,547	
Height (m)	1,67±0,08	170 (140-182)	1,67±0,10	165 (120-190)	1,67±0,09	168 (120-190)	4981	0,935	
BMI (kg/m <sup>2</sup> )	25,87±4,75	25,4 (15,7-49,6)	26,27±5,18	25,4 (16,5-43,9)	26,08±4,98	25,4 (15,7-49,6)	4873,5	0,732	
Days of intensive care unit stay	11,72±11,30	7 (2-51)	4,36±3,32	3 (2-17)	7,73±8,81	4 (2-51)	3224,5	<0,001***	
APACHE-II Score	23,72±9,56	22,5 (1-46)	11,69±7,53	10 (0-43)	17,19±10,41	16 (0-46)	1522,5	<0,001***	
SOFA Score	5,79±3,39	5,5 (0-14)	3,20±2,58	3 (0-10)	4,39±3,24	4 (0-14)	2756,5	<0,001***	
Number of Comorbidities	2,75±1,37	3 (0-6)	1,95±1,32	2 (0-5)	2,32±1,40	2 (0-6)	3413,5	<0,001***	
NRS-2002	4,54±1,16	4,5 (2-7)	2,95±1,51	3 (0-6)	3,68±1,57	4 (0-7)	2081	<0,001***	
mNUTRIC Score	5,45±1,43	5 (1-9)	3,20±1,56	3 (0-8)	4,23±1,87	4 (0-9)	1491	<0,001***	

APACHE- II, acute physiology and chronic health assessment-II; BMI, body mass index; kg; kilogram; m, meter; mNUTRIC, modified nutritional risk score for critically ill patients; NRS-2002, nutritional risk screening-2002; SOFA, sequential organ failure assessment score; SS, standard deviation; U, Mann Whitney u test;  $\bar{X}$ , mean.

\*\* $p < 0,01$ ; \*\*\* $p < 0,001$

**Table 3**

Correlation coefficient between age, BMI, days of ICU stay, number of comorbidities, NRS-2002 score and mNUTRIC scores, and APACHE-II score and SOFA scores according to individuals' mortality status

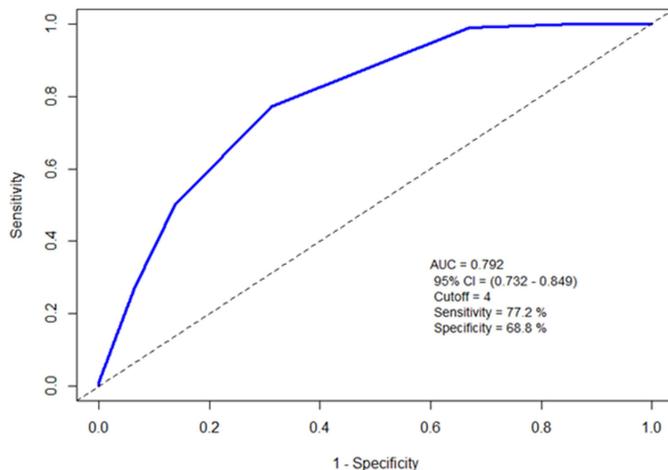
		Mortality Status			
		Yes		No	
		APACHE-II Score	SOFA Score	APACHE-II Score	SOFA Score
Age	s	0,101	-0,311	0,277	-0,065
	p	0,340	0,003**	0,004**	0,499
BMI	s	-0,052	-0,233	0,014	-0,108
	p	0,622	0,025*	0,884	0,266
Days of Intensive Care Unit Admission	s	-0,108	-0,226	0,108	0,014
	p	0,304	0,030*	0,264	0,885
Number of Comorbidities	s	-0,053	-0,111	0,381	0,159
	p	0,619	0,292	<0,001***	0,099
NRS-2002 Score	s	-0,075	-0,103	0,508	0,087
	p	0,476	0,329	<0,001***	0,369
mNUTRIC Score	s	0,728	0,396	0,685	0,344
	p	<0,001***	<0,001***	<0,001***	<0,001***

BMI, body mass index; mNUTRIC, modified nutritional risk score for critically ill patients; NRS-2002, nutritional risk screening-2002; s, spearman's rank correlation coefficient; \* $p < 0,05$ ; \*\* $p < 0,01$ ; \*\*\* $p < 0,001$

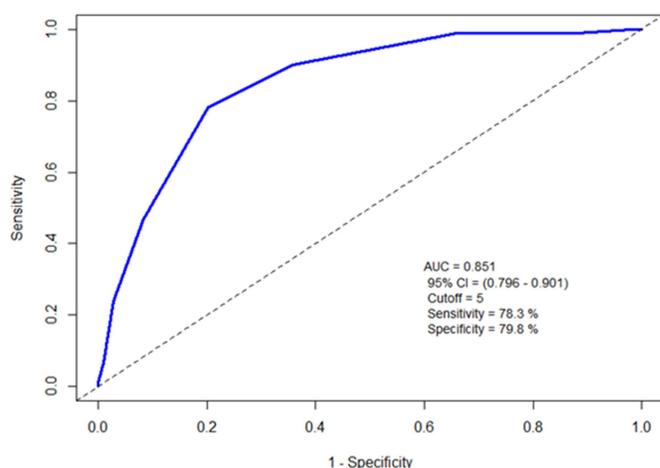
Table 3 presents the correlations between age, BMI, length of ICU stay, number of comorbidities, NRS-2002 score, mNUTRIC score, APACHE II score, and SOFA score according to mortality status. Among non-survivors, mNUTRIC scores showed a strong and statistically significant correlation with APACHE II scores ( $p < 0.001$ ) and a weak but significant correlation with SOFA scores ( $p < 0.001$ ). The results indicated that for non-survivors, each increase in mNUTRIC score was associated with a 72.8% increase in APACHE II score and a 39.6% increase in SOFA score.

**Figure 1**

AUC for the NRS-2002 score predicting mortality rate

**Figure 2**

AUC for the mNUTRIC score predicting mortality rate



Receiver operating characteristic (ROC) analysis was performed to evaluate the ability of the NRS-2002 and mNUTRIC scores to discriminate mortality risk. For NRS-2002, the area under the curve (AUC) was 0.792 (95% CI: 0.732–0.849;  $p < 0.05$ ), with an optimal cutoff value of 4, yielding a sensitivity of 0.772 and a specificity of 0.688. For mNUTRIC, the AUC was 0.851 (95% CI: 0.796–0.901;

$p < 0.05$ ), and the optimal cutoff value was 5, with a sensitivity of 0.783 and a specificity of 0.798. These findings indicate that both screening tools effectively identify patients at mortality risk while minimizing misclassification.

Additionally, our study demonstrated that both NRS-2002 and mNUTRIC successfully detected patients at risk of malnutrition and predicted ICU mortality; however, mNUTRIC exhibited significantly greater predictive accuracy (AUC: 0.851,  $p < 0.001$ ) compared with NRS-2002 (AUC: 0.792,  $p < 0.001$ ) (Figures 1 and 2).

#### 4. Discussion

The aim of this study was to assess the nutritional status of medical ICU patients using the NRS-2002 and mNUTRIC screening tools and to compare their performance in predicting ICU mortality. Among the 201 patients included, 81.6% were at nutritional risk according to NRS-2002 and 25.9% according to mNUTRIC. Among non-survivors, 98.9% were classified as high risk by NRS-2002 and 46.7% by mNUTRIC.

Similar to our findings, a retrospective cohort study from Iran (2021) reported that the mNUTRIC score may effectively identify patients who could benefit from nutritional interventions in the ICU.<sup>19</sup> A recent comparative study evaluating patients with end-stage liver disease showed that both mNUTRIC and NRS-2002 adequately assessed nutritional risk and predicted clinical outcomes.<sup>20</sup> In a Turkish study involving COVID-19 pneumonia patients, 35.9% were identified as high risk by mNUTRIC and 81.4% by NRS-2002, closely aligning with our results.<sup>14</sup> Consistent with the literature, both scores were significantly higher among patients who died in our cohort (NRS-2002: 98.9% vs. 67%; mNUTRIC: 46.7% vs. 8.3%). These findings suggest that both tools are reliable for identifying malnutrition risk in critically ill patients.

Previous studies evaluating NRS-2002 and mNUTRIC have also demonstrated their predictive value for mortality. A 2024 prospective cohort study of 165 critically ill patients comparing five nutritional risk tools found that mNUTRIC and NRS-2002 provided superior prediction of clinical outcomes.<sup>21</sup> Machado Dos Reis et al. (2020) similarly reported a twofold increase in in-hospital mortality among high-risk patients identified by both tools (RR = 2.29; 95% CI: 1.42–3.68;  $p = 0.001$ ), with AUC values of 0.693 for mNUTRIC and 0.645 for NRS-2002.<sup>22</sup> In patients with COVID-19 pneumonia, mNUTRIC also demonstrated better predictive accuracy than NRS-2002 (AUC: 0.875 vs. 0.736;  $p < 0.001$ ).<sup>23</sup> Several additional studies support the strong association between high mNUTRIC scores and increased mortality risk.<sup>24–26</sup>

In line with these findings, our analyses showed AUC values of 0.792 (95% CI: 0.732–0.849) for NRS-2002 and 0.851 (95% CI: 0.796–0.901) for mNUTRIC, indicating that both tools predicted ICU mortality, with mNUTRIC demonstrating significantly higher discriminatory capacity. This may be attributed to the inclusion of key ICU severity indicators within the mNUTRIC score, such as APACHE II and SOFA, which likely reflect the overall clinical condition more accurately.

Studies examining optimal cutoff values for these tools have shown variability across patient populations. In our study, the optimal cutoff was 4 for NRS-2002 (sensitivity 0.772, specificity 0.688) and 5 for mNUTRIC (sensitivity 0.783, specificity 0.798), indicating good ability to identify patients with mortality risk while minimizing misclassification. Supporting this, a large prospective observational study ( $n = 3107$ ) reported an optimal cutoff  $> 4$  for mNUTRIC in predicting 28-day mortality (sensitivity 61.48%, specificity 78.81%).<sup>12</sup> Similarly, a prospective cohort study suggested that

NRS-2002  $\geq 4$  should be considered the critical threshold for predicting ICU mortality.<sup>27</sup> However, Jeong et al.<sup>28</sup> identified a higher cutoff value (6) for mNUTRIC when evaluating septic patients, likely reflecting differences in disease severity and population characteristics. This underscores the need for further research to determine the most appropriate mNUTRIC cutoff for various ICU populations.

#### Limitations

This study has several limitations. First, the single-center design of the study may limit the generalizability of the findings, and although 201 patients were included, validation in larger cohorts is needed. The number of comorbidities and the heterogeneity of ICU admission diagnoses may also have influenced the results. Additionally, APACHE II and SOFA scores were recorded within the first 24 hours of ICU admission; however, these parameters may vary substantially over the course of ICU treatment, potentially affecting their predictive accuracy.

#### Strengths of the Study

This prospective observational study was planned and conducted through a multidisciplinary team approach, and the literature on this topic remains limited. Therefore, the present study provides supportive data for future research and represents an original contribution to the field. Moreover, the inclusion of patients with diverse diagnoses enhances the generalizability of our findings and improves their applicability to the broader ICU population.

## 5. Conclusions

This study demonstrated that both the NRS-2002 and mNUTRIC scores effectively identified patients at risk of malnutrition and predicted ICU mortality, with the mNUTRIC score showing significantly greater predictive accuracy (AUC: 0.851,  $p < 0.001$ ) compared with NRS-2002 (AUC: 0.792,  $p < 0.001$ ). Based on our findings, a cutoff value of  $\geq 5$  for mNUTRIC and  $\geq 4$  for NRS-2002 may serve as useful predictors of mortality in the medical ICU. In addition to medical management, performing nutritional risk screening within the first 24–48 hours of ICU admission and providing individualized nutritional support are crucial for improving clinical outcomes.

#### Statement of ethics

The study protocol was approved by the Ethics Committee of Adana City Training and Research Hospital Clinical Research Ethics Committee on March 11, 2019 (Decision No: 602). Due to the COVID-19 pandemic, additional approval was obtained to extend the study period until 31.03.2021, after which the study commenced. All participants were informed in detail about the study's purpose and procedures, and written informed consent was obtained from each participant in accordance with the Declaration of Helsinki

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#### Conflict of interest statement

The authors declare that they have no conflict of interest.

#### Availability of data and materials

Due to institutional privacy policies, the datasets generated and/or analyzed during the current study are not publicly available, but they are available from the corresponding author upon reasonable request.

#### Author Contributions

D. Dogan and E. Bayraktar equally contributed to the conception and design of the research; A. Özçelik, and H. E. Sümbül contributed to the design of the research; C. Zengin and H.E. Sümbül contributed to the acquisition and analysis of the data; D. Dogan and E. Bayraktar contributed to the interpretation of the data; A. Özçelik, C. Zengin and H.E. Sümbül drafted the manuscript. All authors critically revised the manuscript, agree to be fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript.

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