# RESEARCH



# Effect of the modified NUTRIC score in predicting the prognosis of patients admitted to intensive care units



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## Abstract

**Background** Nutritional deficiency is common in critically ill hospitalized patients. This condition may be aggravated by increased dietary requirements and deficiencies in nutrient absorption. This study aimed to evaluate the associations between the modified Nutritional Risk in Critically ill (mNUTRIC) score and mortality and morbidity in patients with sepsis.

**Methods** In this prospective observational study, 78 patients with sepsis were enrolled in the general intensive care unit over a 3-month period. Demographic and clinical data and laboratory results were recorded and followed up. The nutrition of each patient was started by the nutrition team, and a modified score (mNUTRIC) was calculated. This score was used to assess the patients' nutritional status and mortality risk.

**Results** The mean age of the patients was 77.2  $\pm$  9.9 years, and the majority were men. The median mNUTRIC score was 6. The cohort was divided into two groups: 31 patients (39.7%) with low scores and 47 patients (60.3%) with high mNUTRIC scores. A high mNUTRIC score was associated with an increased need for vasoactive drugs (p < 0.001) and mechanical ventilation (p < 0.001), as well as increased acute kidney injury (p = 0.014) and prolonged hospital stay (p < 0.001) during ICU follow-up. The mNUTRIC score showed high accuracy in predicting mortality (p < 0.001).

**Conclusions** In this study, to predict the prognosis of patients with sepsis in the ICU, the mNUTRIC score was associated with mortality. The inclusion of nutritional assessment scoring tools in the routine clinical evaluation of ICU patients is important.

Keywords Sepsis, Mortality, Intensive care unit, NUTRIC score

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## Introduction

Nutritional deficiency is common among hospitalized patients. When the increased nutritional requirements of critically ill patients in intensive care units (ICUs) due to hypermetabolism and defects in nutrient absorption and utilization are considered, the situation becomes even more severe [1]. Sepsis and septic shock are the leading causes of mortality in patients admitted to the ICU [2]. The consequences of malnutrition in critically ill patients include prolonged hospitalization, nosocomial infections, ventilator dependency, poor functional status at ICU discharge, increased morbidity and mortality, and increased hospital costs [3, 4].

Owing to the association with increased complications, morbidity, and mortality rates, the nutritional status of patients should be evaluated at admission, leading to early recognition of critical patients and the provision of appropriate nutritional support. Compared with patients at low nutritional risk, those at high nutritional risk may benefit more from treatment options [5, 6]. This reduces the incidence of malnutrition and associated complications [7]. The European Society for Clinical Nutrition and Metabolism (ESPEN) and the American Society for Parenteral and Enteral Nutrition (ASPEN) have published guidelines recommending nutritional scores for the early identification of nutritional risk in critically ill patients. However, there is no consensus on the scoring system that should be applied [7, 8].

Most traditional scores do not consider inflammation, which results in hypermetabolic status and sarcopenia in critically ill patients [9]. Heyland et al. argued that nutritional risk should be assessed differently in critically ill patients and framed the Nutritional Risk in Critically Ill Patients Score (NUTRICs) [5]. This score takes into account the response to inflammatory stress and protein catabolism and can identify patients who need more aggressive nutrition. The developed model accounted for age, number of comorbidities, number of days between hospitalization and ICU admission, Acute Physiology and Chronic Health Evaluation (APACHE II) score, Sequential Organ Failure Assessment (SOFA) score, and interleukin-6 (IL-6) level. Accordingly, the patients were divided into two groups: those at high nutritional risk and those at low nutritional risk. As IL-6 is not routinely used in all hospitals, Rahman et al. defined a new version of the score by removing this parameter. The new version, called the modified NUTRIC (mNUTRIC) score, has been validated [10]. The parameters of the mNUTRIC score also provide information regarding prognosis, as they are used in the assessment of mortality. This study aimed to evaluate the prognostic value of the mNUTRIC score in patients with sepsis and the ability of this score to differentiate patients at nutritional risk.

## Methods

In our study, patients admitted to the ICU for sepsis were prospectively observed. The study was approved by the Bolu Abant İzzet Baysal University Clinical Research Ethics Committee (decision no: 2023/237, dated 18 July, 2023) and was conducted in the Bolu İzzet Baysal State Hospital General ICU. The study duration was 3 months (19 July, 2023 to 19 October, 2023). After consent was obtained from the patients and/or their relatives, 78 patients aged>18 years who remained in the ICU for >24 h were included. Patients who were discharged or died within 24 h were excluded.

Demographic data (age and sex), clinical characteristics (comorbidities, vasoactive drug use, renal replacement therapy, mechanical ventilator requirements, development of acute renal failure, and number of days of hospitalization), and laboratory results (complete blood count, albumin, total bilirubin, AST, ALT, creatinine, sodium, potassium, magnesium, and CRP) were recorded within the first 24 h. The patients were followed up until discharge or death in the ICU. Mortality rates were recorded at the end of the follow-up in ICU period.

Each patient was started on enteral/parenteral nutrition by the nutrition team. The energy requirement was calculated at 25–30 kcal/kg.

The mNUTRIC scores of the patients were calculated and used to evaluate their nutritional status and mortality risk. The score includes age, APACHE II score, SOFA score, number of comorbidities, and length of hospitalization before the ICU. Each component was assessed on the basis of a specific score. The total score can range from 0 to 9 points, and a score of 5 points and above is considered a high NUTRIC score.

To summarize the data obtained from the study, descriptive statistics were utilized. For continuous (numeric) variables, on the basis of their distribution, the results are presented in table format either as the mean±standard deviation or as the median, minimum, and maximum. Categorical variables were summarized by their counts and percentages. The normality of the numeric variables was assessed via the Shapiro–Wilk, Kolmogorov–Smirnov, and Anderson–Darling tests.

To compare the differences between groups in terms of categorical variables, the Pearson chi-square test was employed for  $2 \times 2$  tables where the expected counts were 5 or above. When the expected counts were less than 5 in those tables, Fisher's exact test was applied. For RxC tables where the expected counts were less than 5, the Fisher Freeman Halton test was used.

For comparisons between two independent groups, if numeric variables showed a normal distribution, the independent samples t test was applied. For numeric variables that did not display a normal distribution, the Mann-Whitney U test was used. The predictive efficacy of the Nutric score was assessed via receiver operating characteristic (ROC) curve analysis. The performance of the predictive model in prognostic evaluations was quantified by the area under the curve (AUC) value.

Cutoff values were chosen to balance sensitivity and specificity. The model's true positive and negative rates were determined via sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV).

Logistic regression analysis was performed to investigate the relationships among the Nutric score, various clinical conditions, and ICU patient mortality outcomes.

 Table 1
 Descriptive statistics of demographic and clinical characteristics in intensive care unit patients and pairwise comparisons in terms of mortality during follow-up

	Overall	erall Mortality		
	(n=78)	Survived (n=41)	Non- survived (n=37)	
Age (Years) <sup>†</sup>	$77.2 \pm 9.9$	$75.0 \pm 9.3$	79.6±10.1	0.038***
Gender <sup>‡</sup>				
Female	42 (53.8)	20 (48.8)	22 (59.5)	0.473*
Male	36 (46.2)	21 (51.2)	15 (40.5)	
<b>Comorbidities</b> <sup>‡</sup>				
Diabetes Mellitus, present	24 (30.8)	8 (19.5)	16 (43.2)	0.043*
Hypertension, present	23 (29.5)	12 (29.3)	11 (29.7)	0.999*
Heart Disease,	14 (17.9)	8 (19.5)	6 (16.2)	0.934*
Chronic Obstructive Pulmonary Disease (COPD), present	20 (25.6)	12 (29.3)	8 (21.6)	0.608*
Malignant Tumor, present	11 (14.1)	5 (12.2)	6 (16.2)	0.854*
Neurological Dis- ease, present	28 (35.9)	16 (39.0)	12 (32.4)	0.712*
Nutrition Assess-	6.0	4.0	6.0	< 0.001**
ment Score <sup>§</sup>	[2.0-8.0]	[2.0-8.0]	[2.0-8.0]	
Low Score <sup>‡</sup>	31 (39.7)	27 (65.9)	4 (10.8)	< 0.001*
High Score <sup>‡</sup>	47 (60.3)	14 (34.1)	33 (89.2)	
Vasoactive Drug Use, yes <sup>‡</sup>	48 (61.5)	17 (41.5)	31 (83.8)	<0.001*
Renal Replacement Therapy Status, yes <sup>‡</sup>	18 (23.1)	3 (7.3)	15 (40.5)	0.001*
Mechanical Ventila- tion Requirement, ves <sup>‡</sup>	52 (66.7)	18 (43.9)	34 (91.9)	<0.001*
Acute Kidney Injury, present <sup>‡</sup>	32 (41.0)	11 (26.8)	21 (56.8)	0.014*
ICU Stay Duration (Days) <sup>§</sup>	14.0 [4.0–35.0]	9.0 [4.0–29.0]	18.0 [5.0–35.0]	<0.001**

+: II (%), 1: Medit±Stanuaru Deviation, 3: median [Mint-Ma

\*. Pearson Chi-Square or Fisher's Exact test

\*\*. Mann-Whitney U test

\*\*\*. Independent Samples T-Test

Univariate analysis revealed preliminarily significant associations, whereas multivariate analysis refined these relationships, adjusting for potential confounders.

The Kaplan–Meier survival analysis was used to present the survival probabilities on the basis of patients' nutritional scores, illustrating the survival impact of categorical variables in ICU contexts.

Statistical analyses were conducted via the Jamovi (Version 2.3.28) and JASP (Version 0.17.3) software programs. A significance level of 0.05 (p value) was used for the statistical evaluations.

## Results

The average age of patients admitted to the intensive care unit was 77.2±9.9 years. The study included 78 patients, including 42 females (53.8%) and 36 males (46.2%). Comorbidities were present in significant proportions, with 24 patients (30.8%) suffering from diabetes, 23 (29.5%) from hypertension, 14 (17.9%) from heart disease, 20 (25.6%) from COPD, 11 (14.1%) from malignant tumors, and 28 (35.9%) exhibiting neurological comorbidities. The median Nutric score was 6, segregating the cohort into 31 patients (39.7%) with low scores and 47 patients (60.3%) with high Nutric scores. Critical interventions were common, with 48 patients (61.5%) necessitating the use of vasoactive drugs and 18 (23.1%) receiving renal replacement therapy. Upon admission to the intensive care unit, 52 patients (66.7%) required mechanical ventilation, and 32 (41.0%) were diagnosed with acute kidney injury. The median duration of hospital stay was 14 days (refer to Table 1 for additional details).

During the observation period in the intensive care unit, several factors were significantly associated with higher mortality rates. These included older age, a greater incidence of diabetes mellitus (DM), greater nutritional score values, a greater proportion of patients with elevated nutritional scores, increased utilization of vasoactive drugs, more frequent renal replacement therapy, a greater incidence of mechanical ventilation requirements, a greater occurrence of acute kidney injury, and extended hospital stays (p < 0.05 for all mentioned parameters). In contrast, factors such as sex and the presence of other comorbidities, including hypertension (HT), cardiac disease, chronic obstructive pulmonary disease (COPD), malignant tumors, and neurological disorders, were not significantly different between the nonsurvivor and survivor groups (p > 0.05 for each). These findings further emphasize the multifactorial nature of outcomes in intensive care settings (detailed statistics are available in Table 1).

Notably, hemoglobin and albumin levels were significantly lower in the nonsurvivor group than in the survivor group (p=0.009 and p<0.001, respectively). In contrast, other hematological and biochemical indices  
 Table 2
 Descriptive statistics of hematological and biochemical parameters in ICU patients and pairwise comparisons for mortality during follow-up

	Overall	Mortality	p-values*	
	(n = 78)	Survived (n=41)	Non- survived (n=37)	
Hemoglobin (g/dL)§	9.9 [6.3– 16.0]	11.0 [6.6–16.0]	9.2 [6.3–16.0]	0.009
White Blood Cell Count (/µL) $^{\$}$	12.0 [2.8– 32.0]	11.2 [4.0–26.0]	12.0 [2.8–32.0]	0.465
Lymphocyte Count (/µL) <sup>§</sup>	0.9 [0.1–2.3]	0.9 [0.2–2.0]	0.6 [0.1–2.3]	0.437
Platelet Count (/μL) <sup>§</sup>	200.5 [11.0– 527.0]	202.0 [73.0– 444.0]	199.0 [11.0– 527.0]	0.525
Albumin (g/dL) $^{\S}$	24.0 [17.0– 39.0]	26.0 [19.0–39.0]	22.0 [17.0–38.0]	< 0.001
Total Bilirubin (mg/ dL) <sup>§</sup>	0.9 [0.3–5.0]	0.9 [0.3–2.6]	0.9 [0.5–5.0]	0.441
<b>ALT (U/L)</b> <sup>§</sup>	23.0 [5.0– 238.0]	25.0 [5.0–238.0]	22.0 [5.0–170.0]	0.752
<b>AST (U/L)</b> §	24.5 [5.0– 166.0]	21.0 [11.0– 166.0]	26.0 [5.0–165.0]	0.122
Creatinine (mg/dL) $^{\$}$	1.1 [0.3–2.9]	1.1 [0.5–2.3]	1.1 [0.3–2.9]	0.605
Sodium (mEq/L) <sup>§</sup>	139.0 [126.0– 166.0]	140.0 [126.0– 166.0]	138.0 [126.0– 150.0]	0.495
Potassium (mEq/L) <sup>§</sup>	3.9 [2.8–5.5]	4.0 [2.8–5.1]	3.9 [2.8–5.5]	0.353
Magnesium (mEq/L) $^{\$}$	2.0 [1.2–4.0]	2.0 [1.3–4.0]	2.0 [1.2–2.5]	0.553
C-Reactive Protein (mg/dL) <sup>§</sup>	90.5 [5.0– 169.0]	70.0 [7.0–169.0]	99.0 [5.0–154.0]	0.126

§: median [Min.-Max.]

\*. Mann-Whitney U test

did not significantly differ between the groups (p>0.05 for each), underscoring the particular impact of specific nutritional and hematological factors on patient outcomes (refer to Table 2 for a detailed breakdown).

Patients in the intensive care unit with higher Nutric scores demonstrated a significantly increased incidence of acute kidney injury, the need for vasoactive drugs, 
 Table 3
 Comparison of mortality and serious clinical parameters according to nutric score categories

		Nutric sco category	p-values*	
		Low Score (n=31)	High Score (n=47)	-
$Mortality^{\ddagger}$	Survived Non-survived	27 (87.1) 4 (12 9)	14 (29.8) 33 (70.2)	< 0.001
Acute Kidney Injury‡	Absent	26 (83.9)	20 (42.6)	0.001
	Present	5 (16.1)	27 (57.4)	
Vasoactive Drug Use <sup>‡</sup>	No	21 (67.7)	9 (19.1)	< 0.001
	Yes	10 (32.3)	38 (80.9)	
Mechanical	No	18 (58.1)	8 (17.0)	< 0.001
Ventilation Requirement <sup>‡</sup>	Yes	13 (41.9)	39 (83.0)	

‡: n (%)

\*. Pearson Chi-Square or Fisher's Exact test

and the need for mechanical ventilation. Furthermore, these patients exhibited a markedly higher mortality rate ( $p \le 0.001$  for each of these criteria). (Table 3).

The predictive capacity of the Nuntric score was evaluated through receiver operating characteristic (ROC) analysis, which revealed substantial prognostic efficacy across multiple critical conditions. For mortality prediction, an AUC value of 0.788 was achieved, indicating a high level of accuracy. When a cutoff value of >5 was used, the model demonstrated an accuracy rate of 76.92%, with a PPV of 70.21%, an NPV of 87.10%, a sensitivity of 89.19%, and a specificity of 65.85% (p<0.001), highlighting its reliability in clinical scenarios (Table 4).

Similarly, the need for vasoactive drug use was effectively predicted, with an AUC of 0.772. With a more conservative cutoff of >4, the predictive model maintained a robust accuracy rate of 78.21%, a PPV of 79.25%, an NPV of 76.00%, a sensitivity of 87.50%, and a specificity of 63.33% (p<0.001), confirming its utility in predicting this specific intensive care requirement (Table 4).

The analysis extended to the prediction of mechanical ventilation necessity, where the model exhibited an AUC of 0.739. With a cutoff value of >5, the accuracy rate was 73.08%, complemented by a PPV of 82.98%, an NPV of 58.06%, a sensitivity of 75.00%, and a specificity of 69.23% (p=0.001), indicating a balanced predictive capability (Table 4).

Table 4 ROC Analysis Outcomes of Nutrition Assessment Score for various clinical endpoints

Nutrition Assessment Score	AUC	Accuracy (%)	PPV (%)	NPV (%)	Sensitivity (%)	Specificity (%)	Cut Off	95% CI	р
Mortality	0.788	76.92	70.21	87.10	89.19	65.85	>5	0.681-0.872	< 0.001
Vasoactive Drug Use	0.772	78.21	79.25	76.00	87.50	63.33	>4	0.663-0.859	< 0.001
<b>Mechanical Ventilation Requirement</b>	0.739	73.08	82.98	58.06	75.00	69.23	>5	0.627-0.832	0.001
Acute Kidney Injury	0.674	67.95	57.45	83.87	84.37	56.52	>5	0.558–0.776	0.004

AUC: Area Under the Curve, PPV: Positive Predictive Value, NPV: Negative Predictive Value, CI: Confidence Interval

	Univariate Logistic Regression		Multivariate Lo- gistic Regression	
	OR. [95%Cl]	<i>p</i> -values	OR. [95%CI]	<i>p</i> -val- ues
Albumin (g/dL)	0.78 [0.68–0.89]	< 0.001	0.81 [0.69–0.96]	0.016
Vasoactive Drug Use	7.29 [2.50–21.32]	< 0.001	1.07 [0.23–4.98]	0.927
Mechanical Ventilation Requirement	14.48 [3.82–54.86]	<0.001	8.11 [1.68–39.21]	0.009
Nutrition Assess- ment Score: High Score vs. Low Score	15.91 [4.69–54]	< 0.001	9.79 [2.25–42.6]	0.002

 
 Table 5
 The effect of nutric score and clinical conditions on mortality in intensive care unit patients

OR: Odds Ratio, CI: Confidence Interval

Finally, the forecast of acute kidney injury had an AUC of 0.674. At a similar cutoff value of >5, the model's accuracy was slightly moderated at 67.95%, accompanied by a PPV of 57.45%, an NPV of 83.87%, a sensitivity of 84.37%, and a specificity of 56.52% (p=0.004) (Table 4).

A comprehensive logistic regression analysis was conducted to ascertain the influences of the nutritional score and various clinical conditions on mortality outcomes in intensive care unit patients. The univariate analysis revealed significant associations between mortality and several key factors, including albumin levels, vasoactive drug utilization, the need for mechanical ventilation, and classification within the high nutritional score category (p<0.001 for each). Remarkably, a one-unit elevation in the serum albumin concentration correlated with a 22% decrease in mortality risk. Conversely, the initiation of vasoactive drugs, the imposition of mechanical ventilation, and inclusion in the high nutritional score bracket were implicated in mortality risk increases by factors of 7.29.

Subsequent multivariate analyses nuanced these findings. While the use of vasoactive drugs diverged significantly (p=0.927), the remaining variables preserved their critical roles. Specifically, each unit increase in the serum albumin concentration was associated with a 19% reduction in mortality. In stark contrast, the necessities of mechanical ventilation and categorization in the high-Nutric score echelon were potentiated, increasing mortality risk by 8.11 and 9.79 times, respectively.

These insights, consolidated in Table 5, underscore the multifaceted nature of mortality determinants in intensive care contexts, with nutritional status, emergent clinical interventions, and severity assessments via the Nutric score proving pivotal.

As depicted in Fig. 1, the Kaplan–Meier survival curves distinctly demonstrate a significant divergence in survival probabilities within the intensive care context, contingent upon patients' Nutric scores. Notably, individuals with lower nutritional scores had a greater likelihood of prolonged survival than did those with elevated scores (p<0.001). This statistically significant disparity, derived from Kaplan–Meier analysis, highlights the critical prognostic implications of Nutric scores, suggesting their consideration as substantial determinants in patient survival projections and consequent healthcare strategizing within intensive care units.



Fig. 1 K–M survival curves for intensive care unit survival times in the low- and high-nutrient score groups

## Discussion

The importance of nutritional assessment for critically ill patients has increased in recent years. To predict the prognosis of critically ill patients with sepsis in the ICU, this study aimed to determine the effectiveness of using the mNUTRIC score. Patients were classified as having high (60.3%) or low (39.7%) mNUTRIC scores. We aimed to assess nutritional risk in patients admitted to the ICU and demonstrate the use of the mNUTRIC score as a convenient method to predict patient prognosis.

The power of the mNUTRIC score for assessing disease severity and patient prognosis in patients with sepsis in our study was consistent with the broader literature on this topic. The findings of our study were consistent with the reported associations of the use of vasoactive drugs, the need for renal replacement therapy, the need for mechanical ventilation, and the length of ICU stay with mortality [11, 12]. Mahmoodpoor et al. investigated 445 patients and reported that the mNUTRIC score was strongly associated with ICU mortality and vasopressor use; however, its ability to determine the length of hospital stay was poor [13]. In their study of postoperative patients in the care unit, Ozbilgin et al. reported a significant correlation between the NUTRIC score and the development of atrial fibrillation, renal failure, inotropic agent requirements, and mechanically ventilated (MV) requirements [14]. In a retrospective analysis of the predictive power of the NUTRIC and mNUTRIC scores for 28-day ICU mortality, Jeong et al. reported no significant difference between the two scores. They characterized the mNUTRIC score as a good assessment tool, with an AUC of 0.757 (95% CI: 0.713-0.801) [15]. Welna et al. reported that a high NUTRIC score was associated with increased mortality and the need for MV, renal replacement therapy, and steroids and blood products in patients with sepsis admitted to the ICU. The nursing workload was found to be greater in patients with high NUTRIC scores [16]. Kucuk et al. reported that the need for invasive MV, acute kidney injury, and vasopressor use was greater in patients with high NUTRIC scores who were followed-up in the ICU due to COVID-19. In the same study, the NUTRIC score was not found to be superior to the mNUTRIC score [17].

According to the results of the multivariate logistic regression analysis performed to determine the effects of various clinical conditions and the mNUTRIC score on mortality outcomes in ICU patients, the use of vasoactive drugs was not statistically significant (p=0.927), whereas the need for MV and being categorized into a high mNU-TRIC score maintained their critical role (p=0.009, p=0.002). The requirement for MV and categorization in the high-mNUTRIC score stratum increased the mortality risk by 8.11 and 9.79 times, respectively. The multivariate analysis of high mNUTRIC scores in different studies

was similar to that in our study [18, 19]. Mendes et al., in their multicenter study involving 15 ICUs, reported that patients with a score  $\geq$ 5 had higher 28-day mortality. A NUTRIC score  $\geq$ 5 was associated with prolonged ICU stay and a decreased MV requirement [20].

The predictive capacity of the NUTRIC score was evaluated by receiver operating characteristic (ROC) curve analysis, and significant prognostic efficacy was determined in multiple critical conditions. In the mortality prediction analysis, the AUC was 0.788, indicating a high level of accuracy. Our findings demonstrate the power of the modified NUTRIC score for prognostic assessment, especially in patients followed in the ICU.

Our study had several limitations. Although data from 78 patients were evaluated, the number of patients could have been greater in this prospective study. There was no randomization because this was an observational study. Furthermore, this was a single-center study. Additionally, frailty and malnutrition may have affected each other, and we were unable to assess the frailty status of the patients.

## Conclusion

The mNUTRIC score is a useful tool that is easier to compute, and its association with mortality has been demonstrated in several studies. This study, which aimed to predict the prognosis of patients with sepsis in the ICU, revealed that the mNUTRIC score was associated with mortality. Our study contributes to the growing body of evidence emphasizing the importance of nutritional assessment, especially the mNUTRIC score, in ICU patients. Given the important implications of these findings, it would be worthwhile to include nutritional assessments in routine clinical evaluations of ICU patients.

## Abbreviations

mNUTRIC	Modified Nutritional Risk in Critically ill
NUTRICs	Nutritional risk in critically ill patients score
ICU	Intensive care unit
ESPEN	The European Society for Clinical Nutrition and Metabolism
ASPEN	The American Society for Parenteral and Enteral Nutrition
APACHE II	Acute Physiology and Chronic Health Evaluation
SOFA	Sequential Organ Failure Assessment
IL-6	Interleukin-6
DM	Diabetes mellitus
HT	Hypertension
COPD	Chronic obstructive pulmonary disease
ROC	Receiver operating characteristic
AUC	Area under the curve
PPV	Positive predictive value
NPV	Negative predictive value
MV	Mechanical ventilator

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#### Author contributions

MY, ZSY and MD equally contributed to the conception and design of the research. MY, ZSY and MD contributed to the acquisition of the data. MY, ZSY and MD contributed to the analysis and interpretation of the data. MY,

ZSY and MD drafted the manuscript. All authors read and approved the final manuscript.

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#### Data availability

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

## Declarations

#### Ethics approval and consent to participate

The Bolu Abant İzzet Baysal University Clinical Research Ethics Committee approved this study with the ethical code 2023/237. Written informed consent was received from all subjects or their care givers before beginning the study. All methods were carried out in accordance with relevant guidelines and regulations or Declaration of Helsinki.

#### **Consent for publication**

Not applicable.

#### **Competing interests**

The authors declare no competing interests.

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