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# **CONUT Score as a Potential Nutritional Index for Predicting Mortality among Septic Patients**

Septik Hastalarda Mortaliteyi Öngörmede Potansiyel Bir Nutrisyonel İndeks Olarak CONUT Skoru

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#### **ABSTRACT**

**Objective:** In sepsis patients, impairment of the immune system can damage the ability of fighting infection, and leads to poor outcomes. The aim of our study is to evaluate the role of the Controlling Nutritional Status (CONUT) score in predicting mortality in sepsis patients, in comparison with other nutritional assessment tools and disease severity scoring systems in intensive care units.

Method: In this retrospective single-centre observational study patients aged ≥18 years who were followed up in intensive care units with a diagnosis of sepsis between January 2016 and October 2024 were included. Data was obtained from files and the hospital's electronic database. Demographic data, laboratory parameters, Acute Physiology and Chronic Health Evaluation II (APACHE II) score, Sequential Organ Failure Assessment (SOFA) score, Nutritional Risk Screening 2002 (NRS 2002), and CONUT scores were recorded. Logistic regression analysis and multivariate modeling were performed to calculate the risk of mortality. The accuracy of APACHE II, SOFA, NRS 2002, and CONUT scores in predicting mortality was compared by receiver-operating characteristic (ROC)

**Results:** The study included 926 patients. In logistic regression analysis, SOFA, CONUT, APACHE II, and NRS 2002 Scores were independent risk factors. The CONUT score (AUC: 0.974), SOFA score (AUC: 0.964) and APACHE II score (AUC: 0.938) showed higher diagnostic accuracy than the NRS 2002 score (AUC: 0.814). There was no significant difference between CONUT and SOFA scores (p=0.37; z=1.48). CONUT score had a higher AUC than APACHE II (p<0.05; z=4.15).

**Conclusion:** The CONUT score offers a practical alternative to clinicians, especially in assessing nutritional status and predicting mortality in patients with sepsis, due to its easy applicability and reliance on biochemical parameters.

**Keywords:** Sepsis, malnutrition, mortality, CONUT score, NRS 2002 score

#### ÖZ

Amaç: Sepsis hastalarında, yetersiz beslenmeye bağlı bağışıklık sisteminin zayıflaması enfeksiyonla mücadele yeteneğini engelleyerek kötü sonuçlara yol açabilir. Çalışmamızın amacı, hem beslenme hem de inflamasyonla ilgili parametreleri içeren Beslenme Durumu Skoru (CONUT) skorunun sepsis hastalarında mortaliteyi tahmin etmedeki rolünü, yoğun bakım ünitelerinde rutin olarak kullanılan beslenme değerlendirme araçları ve diğer hastalık şiddeti puanlama sistemleriyle karşılaştırmaktır.

Yöntem: Retrospektif tek merkezli gözlemsel olan bu çalışmada yoğun bakım ünitelerinde 2016 Ocak ve 2024 Ekim tarihleri arasında sepsis tanısıyla takip edilmiş olan 18 yaş üstü hastalar dosyalarından ve hastane elektronik veri tabanından taranmıştır. Hastaların demografik verileri, laboratuvar parametreleri, Akut Fizyoloji ve Kronik Sağlık Değerlendirmesi II (APACHE II) ve Sıralı Organ Yetmezliği Değerlendirmesi (SOFA) skorları, Beslenme Risk Taraması 2002 (NRS 2002) ve CONUT puanları kaydedilmiştir. Mortalite riskinin hesaplanması için lojistik regresyon analizi yapılmıştır. APACHE II, SOFA, NRS 2002 ve CONUT skorunun mortaliteyi öngörmeleri alıcı-işletim karakteristik (ROC) eğrileri ile kıyaslanmıştır.

**Bulgular:** Çalışmaya 926 hasta dahil edildi. Lojistik regresyon analizinde SOFA, CONUT, APACHE II ve NRS 2002 skorları bağımsız risk faktörleri olarak belirlendi. CONUT skoru (AUC: 0,974), SOFA skoru (AUC: 0,964) ve APACHE II skoru (AUC: 0,938), NRS 2002 skorundan (AUC: 0,814) daha yüksek tanısal doğruluk gösterdi. CONUT ve SOFA puanları arasında anlamlı bir fark yoktu (p=0,37; z=1,48). CONUT puanı, APACHE II'den daha yüksek bir AUC değerine sahipti (p<0,05; z=4,15).

**Sonuç:** CONUT skoru, ucuz biyokimyasal parametrelerle ölçülmesi, kolay uygulanabilirliği sayesinde sepsis hastalarında beslenme durumunu değerlendirmede ve mortaliteyi öngörmede değerli bir parametredir.

**Anahtar sözcükler:** Sepsis, malnutrisyon, mortalite, CONUT skoru, NRS 2002 skoru

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#### INTRODUCTION

Sepsis is a serious condition that can cause organ failure due to the body's disorganised response to an infection (1). In sepsis, mortality rates are high, and early prediction of mortality is essential for effective treatment. The nutritional status of the patients effects the progression and outcome (2). The malnourished patients have higher complication rates, longer hospital stays, and increased risk of death (3,4). Nutritional assessment tools, such as NUTRIC (Nutrition Risk in Critically III) and NRS 2002 (Nutritional Risk Screening 2002), are commonly used to evaluate the nutritional status of intensive care unit (ICU) patients (5,6).

However, using these scores can sometimes be difficult for clinicians. Because, some of the parameters are not always available, such as weight change, which may be unknown. The CONUT (Controlling Nutritional Status) score, first determined in 2005, is easy for calculation and have objective parameters (7). The CONUT score has been investigated for its impact on nutrition and patient outcomes in a wide variety of disease groups (8-11). There are also some studies evaluating the CONUT score in sepsis patients admitted to intensive care units, but their number is low (12,13).

The CONUT score includes serum albumin level, lymphocyte count, and total cholesterol values (14). The serum albumin level reflects nutritional status; however, it may also decrease as part of the acute-phase inflammatory response in sepsis. The lymphocyte count indicates the immune response and the power of the immune system. Total cholesterol is not only crucial for maintaining the structural integrity of cell membranes, but also plays an important role in immunomodulation and the synthesis of steroid hormones, including adrenal corticosteroids (15). In the context of sepsis, hypocholesterolemia has been associated with impaired immune responses, increased disease severity, and poor clinical outcomes. The CONUT score is calculated based on three laboratory parameters: serum albumin, total lymphocyte count, and total cholesterol levels, each reflecting different aspects of nutritional and immune competence (12,16).

While the impact of the CONUT score on nutritional status and other clinical outcomes has been investigated in various diseases and patient groups, such as cancer, surgical, and geriatric populations, studies specifically focusing on patients with sepsis are relatively limited (8-13). In this study, we aimed to assess the predictive value of the CONUT score for ICU mortality due to sepsis in patients admitted to intensive care units. Rather than emphasizing nutritional evaluation, the study focused on comparing the CONUT score's ability to predict mortality with routinely used ICU prognostic tools (Acute Physiology and Chronic Health Evaluation II (APACHE II) and Sequential Organ Failure Assessment (SOFA) scores) and the NRS 2002 score in a large patient cohort.

#### MATERIAL and METHODOLOGY

# **Study Design and Patients**

This is a retrospective, single-center observational study conducted in the 3<sup>rd</sup> Level ICUs of our hospital. Patients aged ≥18 years who were diagnosed with sepsis or septic shock at the time of ICU admission between January 2016 and October 2024 were included—patients who developed sepsis after ICU admission were not included. The CONUT and NRS 2002 scores were calculated using laboratory and clinical data obtained within the first 24 hours of ICU admission, to reflect the patients' nutritional and immunological status upon entry to intensive care. The primary outcome of interest was ICU mortality, defined as death occurring during the same ICU hospitalization. Patients' data were reviewed from their files and the hospital's electronic database. Ethical approval was granted on 01.11.2024 with the date and number 28574. Our study was conducted in accordance with the Helsinki Declaration and the Standards for Reporting Diagnostic Accuracy Studies (STARD) guidelines. As the study had a retrospective design, the voluntary informed consent form was withheld.

Patients with a diagnosis of malignancy or known hematologic disease, with intoxication, with dyslipidemia and receiving related treatment, with insufficient clinical and laboratory data, admitted to our ICU while being followed up in another center due to sepsis, and patients with an intensive care unit stay of less than 24 hours were excluded.

# **Descriptions**

# Sepsis Definition

An experienced intensive care specialist diagnosed sepsis according to the Survival in Sepsis Campaign 2021 Guidelines (1). Sepsis was defined by a SOFA score of  $\geq$  2 in patients who met the criteria for infection, and septic shock was defined by the use of vasopressors and lactate levels > 2 mmol L<sup>-1</sup> on admission.

#### NRS 2002

The NRS 2002 score, including parameters such as nutritional status, disease severity, and age, was determined by an experienced intensive care specialist according to the European Society for Clinical Nutrition and Metabolism guidelines (17). The NRS 2002 score is based on a combination of nutritional status, disease severity, and age. The score ranges from 0 to 7, where a total score of 3 or higher indicates a clinically significant risk of malnutrition.

It includes: 0–3 points for impaired nutritional status (based on Body Mass Index (BMI), recent weight loss, and food intake), 0–3 points for the severity of the disease, and +1 point for age  $\geq$ 70 years. Higher scores indicate greater nutritional risk and the need for nutritional intervention.

#### **CONUT** score

It was first reported in the literature by Ulibarri et al. and calculated accordingly (Table I) (14). The CONUT score is based on three biochemical parameters: serum albumin, total lymphocyte count, and total cholesterol levels. Each parameter is assigned a score based on predefined ranges. The total CONUT score ranges from 0 to 12, where higher scores reflect worse nutritional and immunological status. Scores are categorized as: 0–1: Normal nutrition, 2–4: Mild malnutrition, 5–8: Moderate malnutrition, 9–12: Severe malnutrition.

#### **Data Collection**

Patient data were reviewed from patient files and the hospital's electronic record system. Demographic data, including age, gender, body mass index (BMI), Charlson Comorbidity Index, Glasgow Coma Score, APACHE II score, SOFA score, NRS 2002, and CONUT scores, were recorded from the hospital database. The need for mechanical ventilation, renal replacement therapy, and the vasopressor dose were obtained from patient files. Parameters such as complete blood count, urea, creatinine, AST, ALT, glucose, total cholesterol, albumin, C-Reactive protein, and procalcitonin were recorded from the hospital database.

#### **Statistical Analysis**

The analyses were evaluated using the SPSS (Statistical Package for the Social Sciences; SPSS Inc., Chicago, IL) 26 package program. Descriptive data are presented as n (%) for categorical variables and mean ± standard deviation or median (interquartile range) for continuous variables, depending on distribution. The normality of continuous variables was assessed using the Kolmogorov–Smirnov test and complemented by visual methods (histograms and Q–Q plots). These analyses demonstrated that most continuous variables did not follow a normal distribution; therefore, non-parametric tests were applied where appropriate. Normally distributed variables were compared using the Student's t-test, while non-normally distributed variables were compared using the Mann–Whitney U test. Categorical data were compared using the Chi-square test.

Logistic regression analysis was performed to calculate the risk of mortality. Variables with p<0.10 in univariate analyses, as well as clinically relevant variables reported in prior studies, were included in the multivariate logistic regression model. The final model comprised SOFA, APACHE II, CONUT, and NRS 2002 scores. Odds ratios (ORs) with 95% confidence intervals (CIs) were reported.

Receiver Operating Characteristic (ROC) curve analysis was conducted to evaluate the predictive accuracy of the scoring systems. The area under the ROC curve (AUC) was calculated for each score. Pairwise AUC comparisons were performed using the DeLong method. The level of statistical significance was set at p<0.05.

# **RESULTS**

Between January 2016 and October 2024, 1311 patients over the age of 18 were admitted to our 3<sup>rd</sup>-level ICUs due to sepsis. Ninety-five patients were excluded due to malignancy/hematologic disease, 105 due to dyslipidemia, 107 due to sepsis from another hospital, 55 due to missing data, and 23 due to an ICU duration of less than 24 hours (Figure 1). The study included 926 patients.

Among the patients, 56.3% were female and 43.7% were male, with an overall ICU mortality rate of 38.3%. Mechanical ventilation, vasopressor support, and renal replacement therapy were required in 50.3%, 82.8%, and 39.2% of patients, respectively.

## **Significant Associated Variables by Mortality**

The overall ICU mortality rate was 38.3%. One of the primary aims of this study was to evaluate the predictive power of the CONUT and NRS 2002 scores for ICU mortality in patients with sepsis. The median CONUT score was significantly higher in non-survivors than in survivors (9.00 vs 2.00, p<0.001) indicating a strong association between poor nutritional status and mortality. Conversely, the median NRS 2002 score was paradoxically higher in survivors than in non-survivors (5.00 vs 3.00, p<0.001). When stratified by CONUT score categories, 49.2% of survivors had normal nutritional status and 38.5% had mild malnutrition. In contrast, 54.4% of non-survi-

Table I. CONUT Score

Degree of nutritional deficiency	CONUT Score	Albumin (g dL <sup>-1</sup> )	Lymphocyte (10³ μL <sup>-1</sup> )	Total Cholesterol (mg dL <sup>-1</sup> )
Normal	0-1	≥ 3.50 (0)	≥ 1.600 (0)	≥180 (0)
Mild	2-4	3.00-3.49 (2)	1.200-1.599 (1)	140-179 (1)
Moderate	5-8	2.50-2.99 (4)	800-1.199 (2)	100-139 (2)
Severe	9-12	<2.50 (6)	<800 (3)	<100 (3)

**CONUT:** Controlling nutritional status.

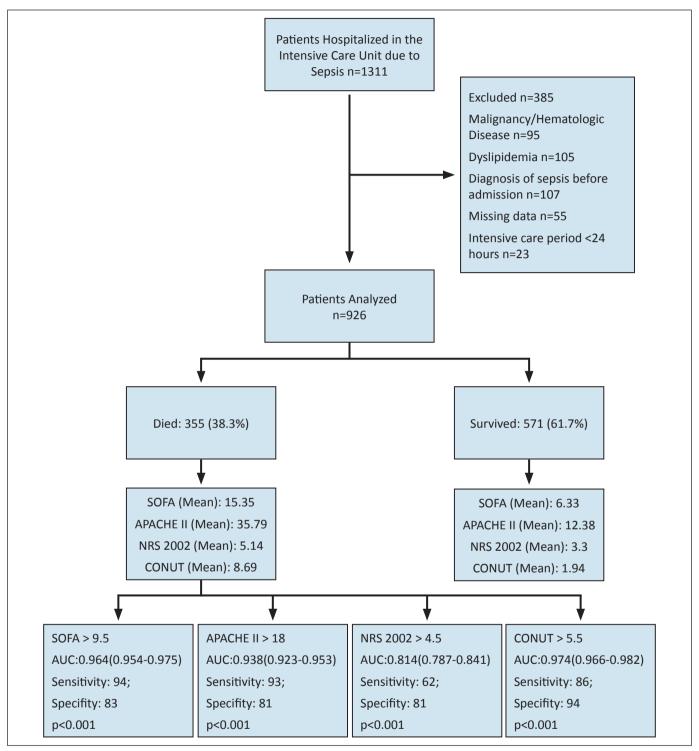


Figure 1. Flow diagram of patient selection and analysis. NRS 2002: Nutritional risk screening 200, CONUT: Controlling nutritional status. SOFA: Sequential organ failure assessment, APACHE II: Acute physiology and chronic health evaluation II.

vors were severely malnourished, and 41.1% were moderately malnourished. Notably, no non-survivor fell into the normal CONUT category, underscoring a strong link between higher CONUT scores and ICU mortality.

In terms of secondary findings, non-survivors were significantly older (median 79 years), and had higher Charlson Comorbidity Index scores, and lower BMI, serum albumin, and cholesterol levels (all p<0.001). Mortality was significantly higher among patients requiring mechanical ventilation

(74.9%), vasopressor support (46.3%), and renal replacement therapy (68.6%) (all p<0.001). The SOFA and APACHE II scores were also significantly elevated in the non-survivor group, indicating the contribution of organ dysfunction and disease severity to poor outcomes.

Finally, of the 767 patients who received vasopressor therapy, all met the Sepsis-3 criteria for septic shock upon ICU admission. However, due to dataset limitations, further subgroup analysis comparing sepsis and septic shock was not possible beyond vasopressor use. Complete comparisons are shown in Table II.

# **Logistic Regression Analysis**

In the logistic regression analysis, the SOFA Score, CONUT

Score, APACHE II Score, and NRS 2002 Score were identified as independent risk factors (Table III).

# Receiver Operating Characteristic (ROC) Curves and Cut-Off Points

The 4 available scores were then further evaluated using ROC analysis (Table IV and Figure 2). The ROC curves were created to assess the diagnostic accuracy of CONUT, NRS 2002, APACHE II, and SOFA scores in predicting ICU mortality. The area under the ROC curve (AUC), optimal cut-off points, sensitivity, and specificity were calculated with the Youden Index. Pairwise AUC comparisons were performed using the DeLong method to determine statistical significance between scores. Although the significance values of all scores were similar,

Table II. Comparison of Demographic, Clinical and Laboratory Characteristics by ICU Mortality

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Variable	Total (n=926)	Survivors (n=571)	Non-survivors (n=355)	p-value*
Age	77 (68–84)	76 (68–83)	79 (71–85)	<0.001
Gender (Female), n (%)	521 (56.3)	323 (56.5)	198 (55.8)	0.813
Mechanical Ventilation, n (%)	466 (50.3)	117 (20.5)	349 (74.9)	<0.001
Vasopressor Use, n (%)	767 (82.8)	412 (72.1)	355 (100)	<0.001
Renal Replacement Therapy, n (%)	363 (39.2)	114 (20.0)	249 (68.6)	<0.001
Age (years), median (min-max)	77 (68–84)	76 (68–83)	79 (71–85)	<0.001
CCI, median (min-max)	2.0 (1-3)	2.0 (1–2)	2.0 (2-3)	<0.001
BMI (kg m <sup>-2</sup> ), median (min–max)	20.9 (19.5–22.8)	21.3 (20.3–23.1)	20.5 (18.9–21.8)	<0.001
GCS, median (min–max)	12 (10–14)	13 (12–14)	10 (9–10)	<0.001
SOFA Score, median (min–max)	9 (5–16)	5 (4–8)	16 (14–18)	<0.001
APACHE II Score, median (min-max)	19 (10–34)	11 (6–16)	33 (25–46)	<0.001
ICU Stay (days), median (min-max)	7 (3–17)	5 (3–11)	10 (4–24)	<0.001
CRP (mg L <sup>-1</sup> ), median (min–max)	6.70 (1.4–18.5)	1.95 (0.92–5.10)	16.10 (11.8–21.7)	<0.001
Albumin (g dL <sup>-1</sup> ), median (min–max)	3.2 (2.6-3.7)	3.60 (3.40-3.80)	2.80 (2.40-3.20)	<0.001
Procalcitonin (ng mL-1), median (min-max)	1.6 (0.1–15.4)	0.08 (0.02-0.78)	10.80 (3.20-22.40)	<0.001
Leukocyte (10³ μL <sup>-1</sup> ), median (min–max)	10.6 (8.1–13.6)	9.00 (7.20-10.90)	12.69 (10.04–15.69)	<0.001
Hemoglobin (g dL <sup>-1</sup> ), median (min–max)	11.2 (9.6–12.9)	12.5 (11.5–13.5)	9.50 (8.30–11.90)	<0.001
Platelets (10 <sup>3</sup> μL <sup>-1</sup> ), median (min–max)	205 (140–270)	232 (179–291)	161 (111–223)	<0.001
Neutrophils (10 <sup>3</sup> μL <sup>-1</sup> ), median (min–max)	8.2 (5.6–10.9)	5.80 (4.60-7.60)	10.19 (8.14–12.68)	< 0.001
Lymphocytes (10³ μL-¹), median (min–max)	1.3 (0.7–2.1)	1.89 (1.45–2.40)	0.80 (0.60-1.23)	<0.001
Monocytes (10³ μL-¹), median (min–max)	0.52 (0.41–0.70)	0.45 (0.36–0.55)	0.66 (0.50-0.85)	<0.001
Cholesterol (mg dL <sup>-1</sup> ), median (min–max)	142 (96–205)	194 (149–256)	82 (75–91)	<0.001
NRS 2002, median (min–max)	4.1 (3-5)	5.0 (4–6)	3.0 (2-4)	<0.001
CONUT, median (min–max)	5.5 (2–9)	2.0 (0-3)	9.0 (7–11)	<0.001

<sup>\*</sup>Mann Whitney U Test, Kolmogorov–Smirnov test, Chi-square test.

**BMI:** Body mass index, **GCS:** Glasgow coma scale, **ICU:** Intensive care unit, **MV:** Mechanical ventilation, **VP:** Vasopressors, **RRT:** Renal replacement therapy, **CRP:** C-Reactive protein, **WBC:** White blood cell, **SOFA:** Sequential organ failure assessment, **NRS 2002:** Nutritional risk screening 2002, **CONUT:** Controlling nutritional status, **APACHE II:** Acute physiology and chronic health evaluation II, **CCI:** Charlson comorbidity index.

Table III. Logistic Regression Analysis

Variable	Univariate OR (95% CI)	p-value	Multivariate OR (95% CI)	p-value
Age	1.024 (1.011–1.036)	<0.001	0.998 (0.944–1.055)	0.939
Charlson	1.769 (1.510–2.073)	<0.001	0.997 (0.661–1.506)	0.990
BMI	0.879 (0.837–0.923)	<0.001	-	-
GCS	0.311 (0.269–0.360)	<0.001	0.559 (0.401–0.780)	0.001
SOFA	1.857 (1.721–2.003)	<0.001	1.562 (1.353–1.804)	<0.001
APACHE II	1.206 (1.178–1.235)	<0.001	1.068 (1.013–1.127)	0.016
NRS 2002	2.382 (2.117–2.681)	<0.001	1.175 (0.775–1.781)	0.447
CONUT	2.814 (2.435–3.252)	<0.001	2.777 (2.137–3.609)	<0.001
MV	225.707 (98.204–518.753)	<0.001	<u>-</u>	_
VP	<ul><li>– (unstable estimate)</li></ul>	0.995	-	-
RRT	9.417 (6.933–12.791)	<0.001		_

BMI: Body mass index, GCS: Glasgow coma scale, SOFA: Sequential organ failure assessment, NRS 2002: Nutritional risk screening 2002, CONUT: Controlling nutritional status, APACHE II: Acute physiology and chronic health evaluation II, B: Beta coefficient, SE: Standart error, Exp (B): Odds ratio, CI: Confidence interval, MV: Mechanical ventilation, VP: Vasopressors, RRT: Renal replacement therapy.

Table IV. Receiver Operating Characteristic Analysis

Score	AUC (95%CI)	p-value	Cut off	Sensitivity	Specifity
CONUT	0.974 (0.966-0.982)	<0.001	5.5	86	94
NRS 2002	0.814 (0.787-0.841)	<0.001	4.5	62	81
APACHE 2	0.938 (0.923-0.953)	<0.001	18	93	81
SOFA	0.964 (0.954-0.975)	<0.001	9.5	94	83

AUC: Area under curve, SOFA: Sequential organ failure assessment, NRS 2002: Nutritional risk screening 2002, CONUT: Controlling nutritional status, APACHE II: acute physiology and chronic health evaluation II.

there was no statistically significant difference in AUC between CONUT and SOFA scores when tested with the DeLong method (p=0.37; z = 1.48). The CONUT score had a significantly higher AUC than the APACHE II score (p<0.05; z=4.15) and the NRS 2002 score (p<0.05; z=11.14). The SOFA and APACHE II scores also had significantly higher AUCs than the NRS 2002 score (p<0.05; z= 10.15 and p<0.001; z=-7.85, respectively). APACHE II, SOFA, and CONUT outperformed NRS 2002 in diagnostic accuracy (Tables IV and V). As shown in Figure 2, the NRS 2002 score was lower than the other scores.

#### **DISCUSSION**

Sepsis is a serious condition that causes organ dysfunction due to the body's systemic response to infection and is linked to high mortality rates. Malnutrition is an important problem in sepsis, and causes worse outcomes (2). In this study, the CONUT score was compared with other disease severity scores, such as APACHE II, SOFA, and NRS 2002. We showed that the CONUT score is an effective tool for predicting mortality in patients with sepsis.

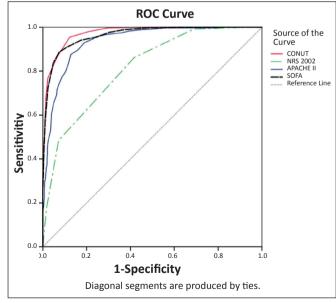


Figure 2. ROC curve.

Table V. Pairwise AUC Comparison Results

Comparison	Z-Value	p-value
CONUT vs SOFA	1.48	0.137
CONUT vs APACHE II	4.15	<0.001
CONUT vs NRS 2002	11.14	<0.001
SOFA vs APACHE II	2.78	0.005
SOFA vs NRS 2002	10.15	<0.001

**SOFA:** Sequential organ failure assessment, **APACHE II:** Acute physiology and chronic health evaluation II, **NRS 2002:** Nutritional risk screening 2002, **CONUT:** Controlling nutritional status.

Nutritional status is an important parameter affecting intensive care patients' prognosis (16). Inadequate nutrition impairs immune system functions, and increases the risk of morbidity and mortality (18). The CONUT score is simple and quick to calculate. Because it includes routine laboratory tests, and it is more practical than the other complex scores. This ease of use can greatly assist clinicians, particularly in making rapid decisions in ICUs.

The Surviving Sepsis Campaign stated that inadequate nutrition in patients with sepsis affects outcomes adversely and emphasized that early enteral nutrition should be initiated (1). Additionally, validated scoring systems are recommended to assess nutritional risk (13,18,19). The NRS 2002 score includes non-quantitative data such as weight loss and reduced dietary intake (10). In contrast, unlike other nutritional assessment indices, the CONUT score reflects the relationship between nutritional status and immune system functioning more objectively by evaluating the nutritional status with laboratory parameters (14,20). Lymphocyte count represents the immune system, albumin level represents protein reserves and dietary deficiencies, and cholesterol represents energy reserves (11,15). The CONUT score has also been reported to show good predictive performance for mortality in patient groups with sepsis (13,21).

Previous studies have shown that decreased lecithin-cholesterol acyltransferase activity due to increased oxidative reactions in sepsis leads to lower cholesterol levels, which then contribute to a poor prognosis (15). It has also been suggested that hypocholesterolemia negatively affects adrenal steroids, vitamin D, and both innate and adaptive immunity (12). Additionally, since albumin also plays a role in cholesterol transport, which influences cell membrane regulation, the significance of the CONUT score in predicting mortality in sepsis patients becomes even greater. Shi et al. evaluated patients with acute pancreatitis and reported that a CONUT score above 7 resulted in a twofold increase in mortality risk (HR: 2.093, 95% CI: 1.342-3.263) (9).

The 926 patients included in our study were mainly elderly. Although a subgroup analysis regarding the CONUT score in elderly patients was not performed in our study, there are findings indicating that the CONUT score predicts mortality in elderly patients (22). In our study as well, mortality was higher in the elderly patient group. When comparing nutritional scores with other critical illness scores, we found a significant rise in APACHE II, SOFA, NRS 2002, and CONUT scores associated with higher mortality. The CONUT score stood out as an independent risk factor in logistic regression, with an Exp(B) value of 2.589 (95% CI: 2.051 - 3.267). This underscores the strong influence of the CONUT score in predicting death. Our findings align with previous research. For example, in a study of COVID-19 patients, a CONUT score above 5.5 was linked to mortality, with an AUC of 0.83 (16). Consistent with this study, in our study, the cut-off value determined for the CO-NUT score was 5.5 and the AUC was 0.974. In a multicenter retrospective study by Baek et al., higher CONUT scores significantly increased 30-day mortality by 2.4 times (95% CI 1.95-3.02) in septic patients (13). Kyo et al. demonstrated a linear relationship between CONUT score and mortality in a multicenter study involving 32159 sepsis patients in Japan (21).

Evaluating CONUT, NRS 2002, APACHE II, and SOFA scores with ROC analysis, we found that the CONUT score demonstrated very high predictability with 86% sensitivity and 94% specificity at a cut-off value of 5.5. When comparing these four scoring methods, the CONUT score had a statistically significantly higher AUC value than APACHE II and NRS 2002.

The CONUT score may offer a reliable prognostic assessment, especially in clinical settings where nutritional status is crucial, such as sepsis. Additionally, although APACHE II considers acute physiologic changes and comorbidities, it does not directly evaluate the patient's nutritional status or immunologic reserves. The APACHE II score indirectly measures the metabolic effects of inflammation and requires a more complex calculation method (23). Therefore, the CONUT score's easy applicability makes it a more practical score.

However, the NRS 2002, includes age, weight loss, food intake, and disease severity. These factors depend on information from the patient, relatives or clinical observations, which can lead to a high subjective error rate (24). So it can be time-consuming and may not be practical for ICU patients who require rapid intervention (25, 26). This makes CONUT more advantageous for clinical decisions regarding acute conditions like sepsis.

Interestingly, the NRS 2002 score was significantly higher in survivors than in non-survivors. One possible explanation is that the NRS 2002 mainly evaluates chronic nutritional risk and incorporates subjective components like recent weight

loss and dietary intake, which may not accurately reflect the acute nutritional status of the patients. In addition, the reliability of NRS 2002 data in ICU settings may be compromised by incomplete or inconsistent documentation, particularly in rapidly deteriorating cases where thorough history-taking is not feasible. These limitations likely contributed to the unexpected scoring pattern observed in our cohort.

The study have several limitations. Having a retrospective observational analysis makes it difficult to establish a causal relationship in the results. The study was conducted at one center, and this can limit the generalizability of the findings. Excluding certain conditions, such as malignancy, hematologic diseases, or immunosuppressive therapy, may have narrowed the patient population and overlooked potential differences of these groups. We did not evaluate the impact of nutritional support strategies on mortality in patients with sepsis, because of retrospective design. Since nutritional support significantly influences mortality outcomes, the absence of data on this aspect may limit the reliability of the results. Changes in biochemical parameters over time could provide valuable prognostic information in patients with sepsis. The lack of dynamic analysis limits the ability of the results to reflect the clinical situation over time.

#### CONCLUSION

In conclusion the CONUT score is a reliable tool for assessing the relationship between nutritional status and mortality in ICU patients with sepsis. This large cohort of sepsis patients study shows that the CONUT score can predict poor outcomes and guide early intervention. Additionally, the CONUT score may be useful in future for routine ICU prognostic scoring systems. We believe it can serve as a practical and quick predictive tool in the treatment process.

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## **AUTHOR CONTRIBUTIONS**

Conception or design of the work: MT, GA

Data collection: FD, OD

Data analysis and interpretation: GA, MT, AA

Drafting the article: GA, AA

Critical revision of the article: GA, MT

Other (study supervision, fundings, materials, etc): GA, AA, MT,

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The author (GA, MT, AA, FD, OD) reviewed the results and approved the final version of the manuscript.

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