

The mNUTRIC Score as a Tool to Predict Mortality and Increased Resource Utilization in Intensive Care Patients with Sepsis.

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Abstract

Background: The mNUTRIC score is a nutrition risk assessment tool. The aim of this study was to evaluate mNUTRIC score ability to predict 28-mortality, icu resource utilization and nursing workload for patients with sepsis and septic shock.

Methods: We performed a secondary analysis of prospectively collected data from a ICU sepsis registry database. The study included adults diagnosed with sepsis or septic shock, admitted from January to December 2014.

Results: The study included 146 patients. In the ROC curve analysis the mNUTRIC score had the ability to predict 28-day mortality with an AUC of 0.833 (95% CI 0.76-0.89). Additionally group of patients with NUTRIC score ≥ 6 points more frequently required vasopressor infusion, mechanical ventilation, renal replacement therapy, thromboprophylaxis and blood products use. Nursing workload was also significantly higher in this group (TISS-28: 36 pts., IQR 33 – 40 vs. 31 pts, IQR 28 – 34, $p < 0.001$).

Conclusion: The mNUTRIC score obtained at admission to the ICU provided a good discriminative value for 28-mortality and makes it possible to identify patients who will ultimately require intense use of ICU resources with an associated increase in the nursing workload during ICU sepsis treatment.

Background

The NUTRIC score (**n**utrition **r**isk in the **c**ritically ill) is a risk assessment tool. It was developed as a tool intended solely for use in patients treated in the intensive care unit (ICU) in order to help identify those who would benefit most from nutritional therapy. The benefit of using the tool is estimated by calculating the change in the survival rate; a lower NUTRIC score is associated with lower mortality. The conceptual model used to develop the NUTRIC score was complex and consisted of parameters describing chronic and acute inflammation, age, general clinical assessment, organ failure assessment, and markers of acute and chronic starvation. ¹ The model was externally validated and a good discrimination confirmed its predictive ability.² Several further studies have shown an association between the NUTRIC score and ICU mortality. It has been observed that, especially patients with high NUTRIC scores may benefit from optimal nutrition, thus improving survival. ³⁻⁵

Validation of the NUTRIC score can be seen primarily in the impact on 28-day mortality or the requirement for prolonged mechanical ventilation in ICU patients. ¹ However, the relationship between the score and the need to use other ICU resources has not been assessed. Patients who require a much greater use of resources during an ICU / hospital stay are patients with sepsis. The analysis done by Jones et al. showed that patients hospitalized for sepsis consumed significantly more hospital resources over a 12-month period compared to patients hospitalized for diseases other than sepsis. ⁶ Full access to hospital resources is extremely important in the context of an unexpected stress test in the ICU, like what has been experienced during the COVID-19 pandemic. However, a steady increase in ICU resource requirements had

been documented even before the global COVID-19 pandemic. The main drivers of the growing demand for intensive care have been observed to be the ageing of the population, the increasing number and complexity of surgical interventions, the implementation of new therapies, and increasing public expectations for the availability and effectiveness of healthcare based on improved outcomes.⁷ Therefore, an additional predictive tool may be useful to make better use of resources in intensive care units. The relationship between the NUTRIC score and the need to use more ICU resources in hospitalized sepsis patients has not been assessed.

The aim of this study was to assess the power of the NUTRIC score in predicting 28-day mortality in patients with sepsis, since a worse prognosis on admission may be associated with the need for more intense use of ICU resources and a correspondingly higher nursing workload. We hypothesized that NUTRIC scoring could have additional use as a tool for predicting increased resource utilization in the ICU.

Methods

Patient population

This study was a secondary analysis of prospectively collected data from a sepsis registry database. The database was built using the clinical and demographic data of patients treated in a 25-bed mixed ICU that provides care in a 996-bed university hospital. The study included adults (> 18 years of age) diagnosed with sepsis or septic shock, admitted from January to December 2014. The exclusion criteria were re-admission to the ICU or stay in the ICU for less than 24 hours.

Ethics

The study was approved by the local ethics committee at the Wroclaw Medical University, approval number KB 23/2015, and complies with the Declaration of Helsinki of the World Medical Association. The need for informed consent was waived by Bioethics Committee of the Wroclaw Medical University

Patient management and data collection

All patients in the study received standard treatment for sepsis or septic shock according to the Surviving Sepsis Campaign guidelines that were in use at the time in the ICU. [12] At least three specialists in anesthesiology and intensive care and four residents provided care for ICU patients during day shifts from 7am to 3pm. Later, care was provided by one specialist in anesthesiology and intensive care and two residents. The nurse to patient ratio of was 1:1 or 1:2 depending on the stability of the patient.

When collecting data for the sepsis registry database, we used the SEPSIS-II criteria, which were the current criterion at the time.⁸ However, for the purpose of this study, the SEPSIS-III criteria were applied retrospectively to the sepsis registry database.⁹ According to the SEPSIS-III definition, sepsis was defined as life-threatening organ dysfunction caused by a dysregulated host response to infection with a sequential organ failure assessment (SOFA) score of at least 2 pts. In the updated database all patients

meeting the SEPSIS-II criteria also met the SEPSIS-III criteria. Septic shock was defined as sepsis with persistent hypotension requiring vasoactive agents to maintain a mean arterial pressure of at least 65 mmHg and having a serum lactate > 2 mmol/L.

All variables required for the calculation of the NUTRIC score were available in the sepsis database, with the exception of the interleukin 6 concentration (IL-6). Due to the unavailability of the IL-6 records in the database, the previously validated, modified version of the scoring (mNUTRIC score) was used for the calculations on the tested sample.¹ The following data collected in the sepsis registry database were used for the calculation of the mNUTRIC score in the present study: age, baseline Acute Physiology and Chronic Health Evaluation II (APACHE II) score, baseline Sequential Organ Failure Assessment (SOFA) score, number of comorbidities, and days from hospital admission to ICU admission. The APACHE II and SOFA scores were calculated in accordance with source publications.^{10 11} Both scores are routinely used for evaluating the severity of the clinical status of patients at the ICU.

In addition, the treatment requirements during the ICU stay were registered in the database and the resource-consuming interventions were the focus of this analysis. The following procedures for managing each patient during the ICU stay were noted: resuscitation and vasoactive medications; mechanical ventilation; renal replacement therapy; nutrition therapy; the administration of corticosteroids, anticoagulants, and blood products; glucose control; and surgery. The quantification of the daily nursing workload for each patient was calculated using the Therapeutic Intervention Scoring System-28 (TISS-28) and the mean index value was recorded in the database.¹²

Statistical analysis

Descriptive statistics included median (interquartile range) for quantitative variables, and frequency (percentage) for qualitative variables. There were no missing data in the database. The T-student test was used for the comparison of continuous variables between the study groups. Categorical variables were analyzed with the chi-squared test, and contingency tables were used to analyze the frequency distribution of categorical variables. Receiver operating characteristic (ROC) curve analysis was used to measure the ability of the NUTRIC score to discriminate between death and survivors by calculating the area under the curve (AUC), including 95% confidence intervals (CI), to determine sensitivity and specificity; the results of the Youden statistics indicated an optimal cut-off value for the NUTRIC score. The Kaplan–Meier curves and the log-rank test were used to assess differences in 28-day survival functions based on the value of the NUTRIC score. Univariate logistic regression was performed to evaluate the association between the baseline NUTRIC, APACHE II, and SOFA scores and 28-day mortality; the results were reported as the odds ratio (OR) with 95% confidence intervals (CI). All statistical analysis was carried out with Statistica, version 13 (StatSoft Inc., Tulsa, OK, USA). A *p* value <.05 was considered statistically significant.

Results

Study sample

During the study period, a total of 332 consecutive patients admitted to the ICU were screened for inclusion/exclusion criteria. Of this, 156 patients met the inclusion criteria. Due to incomplete data, 146 patients were included in the final analysis. The median age in the sample was 66 (IQR 58 - 77) and the majority of patients were male (n=95, 65%). Out of 146 septic patients enrolled, 129 (88%) had septic shock on admission to the ICU. The main causes of sepsis and septic shock were pneumonia (49%), intra-abdominal infection (35%), and urinary tract infection (7%). Patients were transferred from general wards (48%), an operating theater (38%), the emergency department (7%), other hospitals (6%), and the high dependency unit (1%). Most of the patients were admitted in critical condition with the median SOFA score calculated on day 1 at the level of 10 points (IQR 7-13) and with an APACHEII score of 21 points (IQR 15 - 27). The severity of the clinical condition of the patients was also reflected in the high proportion of cases with failure of four or more organs diagnosed on admission to the ICU (51%). The median ICU stay was 10 days (IQR 4 - 23), and the hospital stay was 32 days (IQR 11- 55).

The optimal cut-off point for mNUTRIC

In the ROC curve analysis the mNUTRIC score calculated on admission to the ICU had the ability to predict 28-day mortality with an AUC of 0.833 (95% CI 0.76–0.89, $p < 0.001$; figure 1). The optimal cut-off value for the mNUTRIC score was 6 points, with a sensitivity of 90% and specificity of 63%, and this point was used to divide the study sample for further analysis, i.e. the group of patients with an mNUTRIC score ≥ 6 points and the group with a mNUTRIC score < 6 points.

In addition, a one-way logistic regression analysis was performed to compare the predictive power of the clinical scales computed on admission to the ICU. The mNUTRIC predicted 28-day mortality with an odds ratio of 2.24 (95% CI 1.71 – 2.95, $p < 0.001$), APACHE II alone with an OR 1.21 (95% CI 1.13 – 1.29, $p < 0.001$), and SOFA score alone with an OR 1.43 (95% CI 1.26 – 1.63, $p < 0.001$).

Characterization of groups of patients according to the optimal cut-off point for the mNUTRIC score

Based on the result of the ROC curve analysis and the results of the Younden statistics, the study sample was divided into Group 1 (patients with an mNUTRIC score < 6 points, n=61) and Group 2 (patients with an mNUTRIC score ≥ 6 points, n=85). In the mNUTRIC < 6 group, 64% were male, in the mNUTRIC ≥ 6 group it was 66% ($p = 0.807$). The analysis of the variables used to calculate the mNUTRIC score is shown in Table 1.

Patient management

The nursing manpower in the care of patients was evaluated with the TISS-28 score index, and the obtained results indicated that the nursing workload was significantly greater in the group with an mNUTRIC score ≥ 6 points, compared with an mNUTRIC score of < 6 pts. (TISS-28: 36 pts., IQR 33 – 40

vs. 31 pts, IQR 28 – 34, $p < 0.001$). In patients with an mNUTRIC score ≥ 6 pts., septic shock was diagnosed in 96% of cases and with an mNUTRIC < 6 pts. in 78% ($p = 0.001$). Fluid resuscitation was used in the majority of patients in both groups ($p = 0.154$) and vasopressors had to be administered in almost all patients with an mNUTRIC ≥ 6 pts. (98%) and in 82% of cases with an mNUTRIC score < 6 pts ($p = 0.001$). Mechanical ventilation and renal replacement therapy were more often employed in the treatment of patients with an mNUTRIC ≥ 6 pts than in cases with an mNUTRIC score < 6 pts. (99 vs. 82% and 54 vs. 26%, respectively). Therapy with steroids was required more than twice as often in the group with an mNUTRIC ≥ 6 pts., compared with an mNUTRIC < 6 pts. (68 vs. 31%), and the need for blood products was also much higher (60 vs. 43%). Table 2 compares the frequencies of different treatment requirements on the day of admission to the ICU.

Patients with an mNUTRIC score ≥ 6 points were characterised by a significantly higher ICU (81% vs. 13%, $p < 0.001$) and hospital (81% vs. 28%, $p < 0.001$) mortality rate.

Analysis of survival

The 28-day mortality of the entire study group was 40%. Among the patients who died, the NUTRIC score calculated on ICU admission was ≥ 6 points in 90% of cases. The median value of the mNUTRIC score in Survivors was 4 points (IQR 3 - 6), and in Non-survivors 7 (IQR 6 - 8). The Kaplan–Meier 28-day survival analysis of time to death showed that there was statistical significance between groups with an mNUTRIC score < 6 and ≥ 6 points ($p < 0.001$, log-rank test), (Figure 2).

Discussion

The NUTRIC score is a novel risk assessment tool initially developed to help identify patients who are more likely to benefit from nutritional therapeutic interventions in the ICU setting.¹ The conceptual model for the development of the NUTRIC score incorporated predictor markers of acute starvation, chronic starvation, acute inflammation, and chronic inflammation.¹³ In contrast to many widely used nutritional risk assessments, this score was developed specifically for use in patients admitted to the intensive care unit.^{14–20} A major drawback of the original NUTRIC score was the inclusion of the concentration of interleukin 6 in the scoring as this parameter is not routinely measured in ICU patients and is often unavailable in hospital databases. Therefore, a modified version of the score (mNUTRIC) was later proposed, without taking into account the value of the interleukin 6 concentration.¹ The mNUTRIC score was externally validated using data from a randomized clinical trial database of 1,223 mechanically ventilated ICU patients.²¹ The external validation was repeated in a later study by Rahman et al., who found that the probability of death at day 28 increased by 1.4 (95% CI, 1.3 - 1.5) for every point increase on the mNUTRIC score, confirming the relationship between the mNUTRIC score and mortality.² In the present study the modified version of the NUTRIC score was used, and the IL-6 concentration was not part of the model. In the analyzed cohort, a very good performance of the mNUTRIC score was found in predicting 28-day mortality with an AUC of 0.833 (95% CI 0.76–0.89, $p < 0.001$), and the optimal cut-off value of 6 points was identified with the Youden statistics and used for dividing the studied sample for

further analysis. The group with an mNUTRIC score ≥ 6 points had a significantly higher mortality compared to the group with < 6 points (81% versus 28%, $p < 0.001$). Previously, de Vries et al. validated the predictive ability of the mNUTRIC score using a cohort of 475 mechanically ventilated patients admitted to an ICU in the Netherlands between 2011–2013, and a good discrimination capacity of the tested score was confirmed in the ROC analysis with an AUC of 0.768 (95% CI 0.722 – 0.814).²² Similar results were obtained by Mukhopadhyay et al. in an Asian population of ICU patients, with an AUC of 0.71 for predicting mortality using the mNUTRIC scale.⁴ These results confirmed the ability of the mNUTRIC score to predict mortality in a specific subset of patients with sepsis and septic shock, i.e., a group of patients at high risk of death.

A recently published study found that 48.9 million cases of sepsis were reported worldwide in 2017; there were also 11 million deaths related to sepsis in the same year.²³ These estimates are based on a unique, detailed analysis of death certificates and are global estimates of the incidence of sepsis, including cases of sepsis that have not been treated in a hospital. The highest incidence and mortality from sepsis were estimated in regions with the lowest availability of medical resources, indicating the need for administrative tools to improve ICU resource utilization. So far, a lot of research has been done to find a model to improve access to ICU resources. One of the available methods is the prediction of the ICU length of stay, assuming that this parameter can be related to the intensity of ICU resource utilization. Verburg et al. provided a systemic review of models designed to predict the ICU length of stay, and eleven different models were identified and investigated. The most frequently used predictors in these models were overall disease severity, source of admission, age, use of mechanical ventilation, the Glasgow Coma Score, comorbidities, and organizational predictors. Unfortunately, no model has been assessed as fully competent for planning and identifying unexpectedly long ICU stay or for benchmarking purposes.²⁴ Another approach to improving access to ICU resources is to use disease-specific severity scores. The PIRO (predisposition, insult, response, organ dysfunction) score was used to assess severity and predict resource utilization in ventilator-associated pneumonia (VAP).²⁵ The model was designed as a simple, practical clinical tool for predicting health-care resource utilization based on the length of ICU stay and the duration of mechanical ventilation, and demonstrated greater use of medical resources in patients with high and very high risk of death based on the PIRO prognosis. Yet another approach to predicting the use of ICU resources may be a model designed to predict the use of specific invasive therapies. Recently Sukmark et al. developed a simplified scoring system for predicting major adverse kidney events among patients diagnosed with acute kidney injury (AKI) and treated in the ICU. This simplified clinical score was based on easily available parameters such as the Glasgow Coma scale, tachypnea, vasopressor use, mechanical ventilation use, oliguria, serum creatinine, blood urea nitrogen, hematocrit, and thrombocytopenia. The model performance was adequate when internally validated (AUC under the ROC curve of 0.80) and feasible even in resource-limited settings; however, the model has not yet been externally validated.²⁶ Various models for predicting shock and vasopressor use have also been developed and evaluated. Recently, Kwak et al. used an attention-based deep learning model to predict the need for vasopressor therapy during the first 24 hours of ICU stay. Only vital signs were used in the final model, with heart rate, respiratory rate, and mean arterial pressure contributing the most (AUC of

0.83)²⁷ In a study by Liu et. al., a clustering technique, called fuzzy c-means was employed to develop a model predicting vasopressor requirements for critically ill patients (AUC of 0.81).²⁸ The authors have suggested the existence of a pre-shock state preceding the transition from sepsis to septic shock; detecting this state with the help of the developed model may be useful in resource allocation, especially when ICU availability is constricted. Later, the Medical Information Mart for Intensive Care – III database was used to externally validate the model. Three different machine learning techniques were used, yielding good performance in identifying septic patients who could develop septic shock, with an AUC of 0.93 and median early warning time of 7 hours.^{28,29} A similar approach was employed for predicting the need for intubation.^{30–32} Siu et al. used machine learning to develop a model predicting the need for intubation during the first 24 hours after ICU admission. The parameters required for the model were as follows: blood gas results, the Glasgow Coma Score, respiratory rate, oxygen saturation, temperature, age, and parameters of oxygen therapy. The reported AUC of the model was 0.86 (95% CI 0.85-0.87).³⁰

The approaches presented above often required advanced automated electronic real-time data collection and analysis. This kind of know-how is not always available in an ICU setting. We employed the mNUTRIC score as a simple tool for predicting ICU resource utilization. It is noteworthy that all the parameters necessary to calculate the mNUTRIC (age, baseline APACHE II score, baseline SOFA score, number of comorbidities, and days from hospital admission to ICU admission) are routinely collected or calculated and stored in the hospital records of patients. Using the cut-off point of 6 on the 9-point mNUTRIC scale, we were able to identify a group of patients who significantly more often required intensive use of ICU resources during the entire stay in the ICU. In patients with an mNUTRIC score ≥ 6 pts., septic shock was diagnosed in 96% of cases and with an mNUTRIC < 6 pts. in 78%. For the treatment of shock, fluid resuscitation was used in the majority of patients in both groups and vasopressors had to be administered in almost all patients with an mNUTRIC ≥ 6 pts. (98%) and in 82% of cases with an mNUTRIC score < 6 pts ($p=0.001$). Mechanical ventilation was used in the treatment of almost all (99%) patients with an mNUTRIC ≥ 6 pts and in 82% of cases with an mNUTRIC score < 6 pts ($p=0.018$). The renal replacement therapy to support kidney function was used twice as often in the group with an mNUTRIC ≥ 6 pts. compared to the the group with an mNUTRIC <6 pts (54 vs. 26%, $p = 0.001$). Therapy with steroids was also required more than twice as often in the mNUTRIC ≥ 6 pts group, compared with the group with an mNUTRIC < 6 pts. (68 vs. 31%), and the need for therapy with blood products was much higher (60 vs. 43%). As expected, the nursing workload was greater in the group with an mNUTRIC ≥ 6 pts. as evidenced by the higher TISS-28 score (36 vs. 31 pts.).

In numerous previous studies it has been observed that the mNUTRIC score identifies patients at high risk of malnutrition who are likely to benefit from nutritional therapy during their ICU stay.^{1,2,4} Due to the lack of specific nutritional data, the relationship between mortality, nutritional adequacy and the mNUTRIC score was not assessed in the studied cohort and we acknowledge this as a limitation of the study. With the development of intensive care, the complexity of the organization and structure of these departments has also increased; therefore, the development and use of scoring systems can contribute to improving the allocation of material and human resources. Nursing workload quantification indices are nowadays

one of the fundamental tools in ICU planning and evaluation. Our results indicate the usefulness of the mNUTRIC score as a potential tool for predicting increased resource utilization in the ICU; however, it is a single center analysis with a relatively small sample size and we consider this to be another limitation of the study.

Conclusions

The mNUTRIC score obtained at admission to the ICU provided a good discriminative value for 28-mortality and makes it possible to identify patients who will ultimately require intense use of ICU resources with an associated increase in the nursing workload during ICU sepsis treatment. Our data indicate that the mNUTRIC score may be useful in ICU resource planning, especially in the face of increased demand for intensive care services such as during a global pandemic. However, external validation based on a larger cohort is required before advocating wider use of the mNUTRIC score as an additional tool for ICU resource planning, and our results should, therefore, be interpreted as an argument for such studies.

Abbreviations

APACHE – acute physiology and chronic health evaluation CI – confidence intervals GCS – Glasgow coma scale ICU – intensive care unit mNUTRIC – modified nutrition risk in the critically ill NUTRIC – nutrition risk in the critically ill RRT – renal replacement therapy ROC – receiver operating characteristic SOFA – sequential organ failure assessment

Declarations

Authors contributions:

M. Wełna was involved in the acquisition of data, interpretation of data, writing and revision of the manuscript

A. Kübler was involved in the study design, interpretation of data and the manuscript revision.

W. Goździk was involved in the study design and the manuscript revision.

B. Adamik was involved in the study design, data analysis and the manuscript revision

Conflict of interest:

M. Wełna declares no conflict of interest.

B. Adamik declares no conflict of interest.

A. Kübler declares no conflict of interest.

W. Goździk declares no conflict of interest.

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Tables

Table 1. Analysis of the variables used to calculate the NUTRIC score.

	mNUTRIC ≥ 6 pts (n=85)	mNUTRIC < 6 pts (n=61)	p-value
Age (years)	69 (63 - 80)	61 (50 - 78)	<0.001
APACHE II	24 (21 - 30)	14 (11 - 18)	<0.001
1st day SOFA	12 (10 - 15)	8 (6 - 10)	<0.001
LOS before ICU admission	3 (1 - 8)	2 (0- 13)	0.112
Number of comorbidities	2 (1 - 3)	1(1 - 2)	<0.001

LOS - length of stay

Table 2. Comparison of therapeutic resource requirements for treating septic patients with an mNUTRIC score < 6 and ≥ 6 points.

Parameter	NUTRIC \geq 6	NUTRIC $<$ 6	p-value
Fluid resuscitation n (%)	73 (86)	46 (75)	0.154
Vasopressors n (%)	83 (98)	50 (82)	0.001
Mechanical Ventilation n (%)	84 (99)	53 (87)	0.018
RRT n (%)	46 (54)	16 (26)	0.001
Steroids n (%)	58 (68)	19 (31)	<0.001
Nutrition Therapy n (%)	48 (56)	45 (74)	0.816
Enteral n (%)	31 (65)	28 (62)	
Parenteral n (%)	17 (35)	17 (38)	
Insulin n (%)	50 (59)	38 (62)	0.643
Thromboprophylaxis n (%)	67 (79)	58 (95)	0.001
Blood products n (%)	51 (60)	26 (43)	0.038
Surgery during ICU stay n (%)	29 (34)	20 (33)	0.866

RRT - renal replacement therapy

Figures

Figure 1

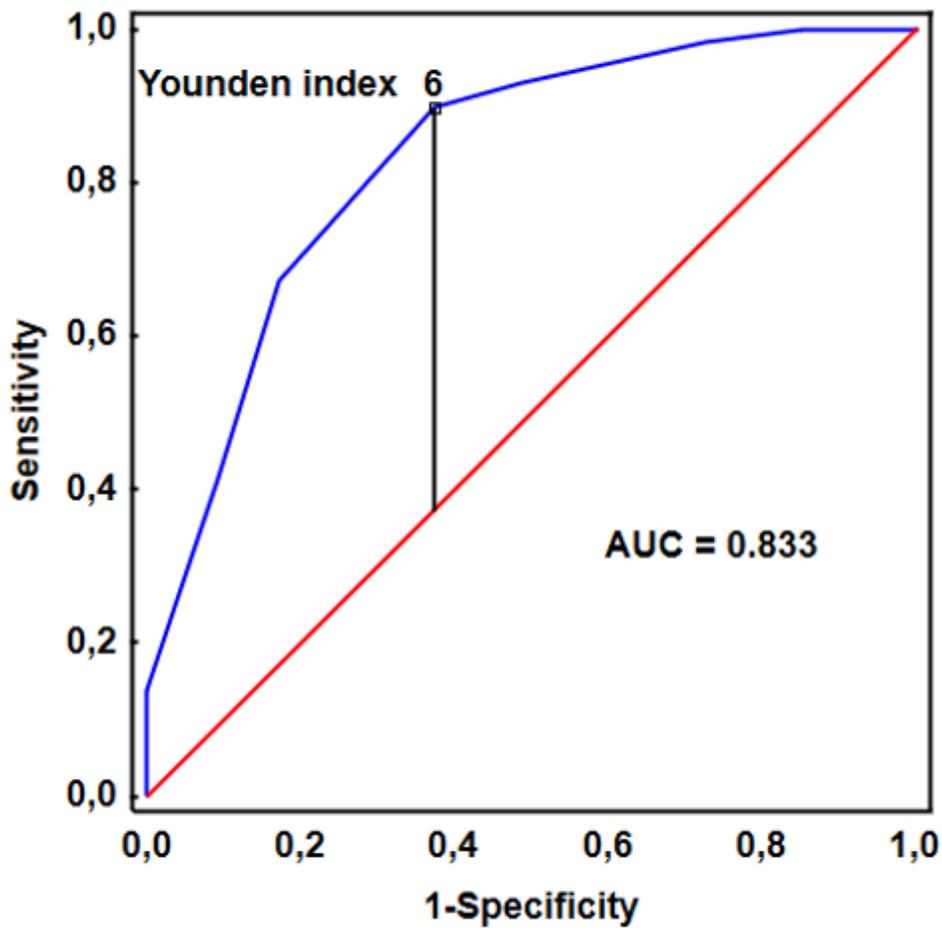


Figure 1

The receiver operating characteristic (ROC) curve illustrates the diagnostic ability of the mNUTRIC score calculated in patients with sepsis on admission to the ICU as a predictor of 28-day survival with an area under the curve (AUC) of 0.833 (95% CI 0.76–0.89, $p < 0.001$). The results of analyzing the Youden statistics indicated the optimal cut-off value for the mNUTRIC score at 6 points.

Figure 2

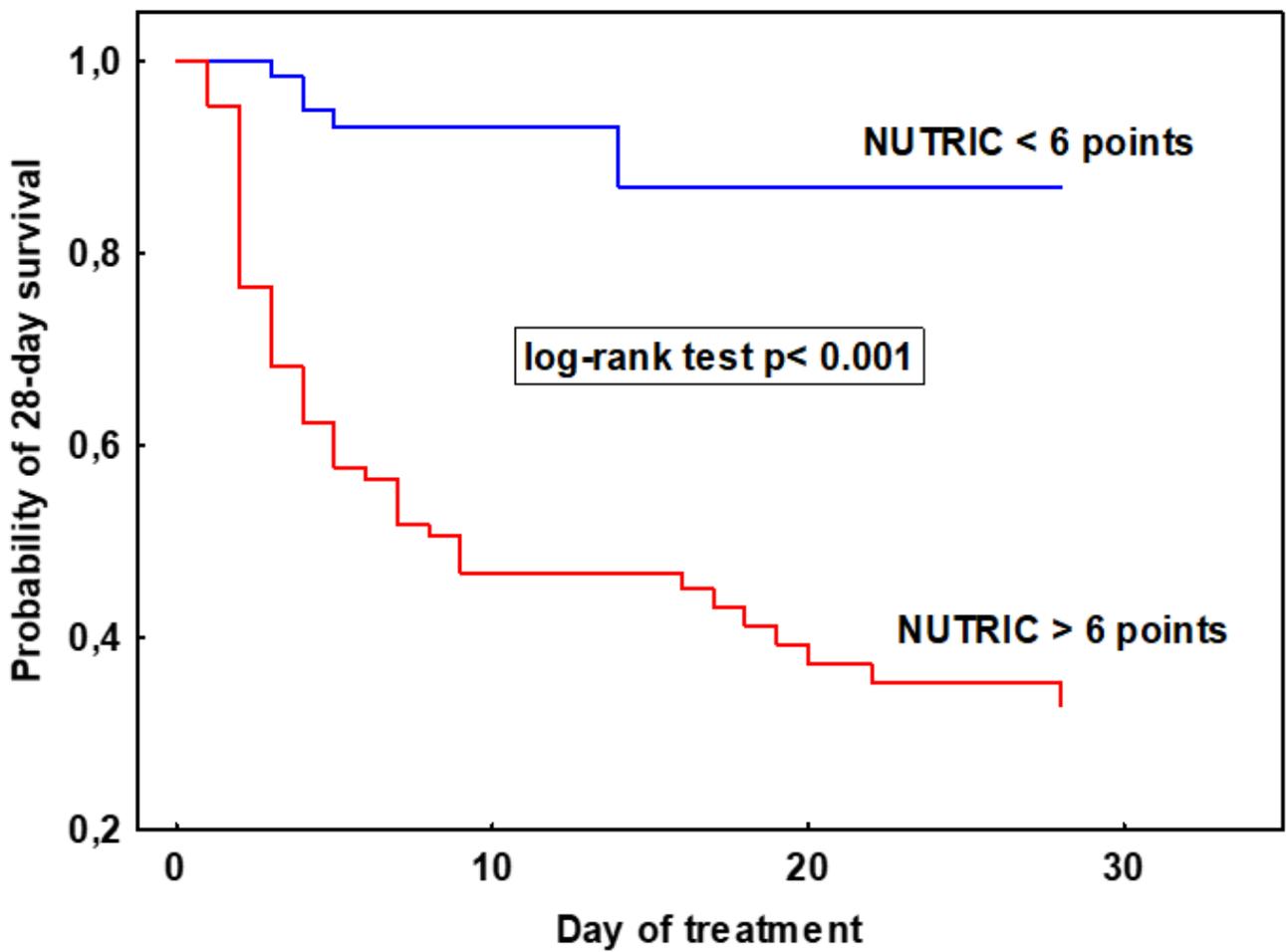


Figure 2

Comparison of 28-day survival in two groups of patients with sepsis on admission to the ICU based on the calculated value of the mNUTRIC score.