SYSTEMATIC REVIEW

Modified NUTRIC Score as a Predictor of All-cause Mortality in Critically Ill Patients: A Systematic Review and Meta-analysis

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Abstract

Purpose: The purpose of our meta-analysis was to look at the impact of modified nutrition risk in the critically ill (mNUTRIC) on mortality in patients with critical illness.

Materials and methods: Literature relevant to this meta-analysis was searched in PubMed, Web of Science, and Cochrane Library till 26 August 2023. Prospective or retrospective studies, patients >18 years of age, studies that reported on mortality and mNUTRIC (mNUTRIC cut-off score) were included. The QUIPS tool was used to evaluate the risk for bias in prognostic factors.

Results: A total of 31 studies on mNUTRIC score, involving 13,271 patients were included. The summary area under the curve (sAUC) of 0.80 (95% CI: 0.76–0.83) illustrates the mNUTRIC score's strong discrimination. The pooled sensitivity was 0.79 (95% CI: 0.74–0.84) and pooled specificity was 0.68 (95% CI: 0.63–0.73). We found no discernible variation in the mNUTRIC's prediction accuracy among cut-off values of <5 and >5 in our subgroup analysis and sAUC values were 0.82 (95% CI: 0.78–0.85) and 0.78 (95% CI: 0.74–0.81), respectively.

Conclusion: We observed that mNUTRIC can discriminate between critically ill individuals and predict their mortality.

Keywords: Critically ill patients, Meta-analysis, Modified NUTRIC score, Mortality prediction, Systematic review.

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Highlights

Intensive care unit (ICU) patients are typically those with acute or chronic disease. Malnutrition in ICU leads to poor response, long-term infection, increased risk for nosocomial infections, and extended ICU stays in patients. The modified Nutrition Risk in the Critically ill (mNUTRIC) is a screening tool for evaluating nutritional risk. There are several studies that have been conducted to evaluate the predictive power of the mNUTRIC on mortality. The results are inconsistent as the population is heterogeneous, the cutoff point is heterogeneous, and clinical settings are heterogeneous. In order to employ the mNUTRIC in evidence-based healthcare settings, it is necessary to evaluate the pooled prediction power on mortality.

Introduction

Nutritional support is an important aspect of the medical treatment provided to critically ill patients. However, there are constraints to using conventional approaches for nutrition assessment in a hospital setting. Malnutrition is believed to afflict one in every three critically ill patients in underdeveloped countries, ranging from 38 to 50% depending on demographics and screening approach.[1–3] Patients admitted to the intensive care unit (ICU) typically have acute or chronic illnesses such as cancer, pneumonia, or sepsis, as well as high catabolic activity in the body. This causes increased release of pro-inflammatory chemicals, oxidative stress, disrupted metabolic activity, and skeletal muscle atrophy, delaying treatment outcomes. Malnourishment in ICU leads to poor response, prolonged infection, risk of nosocomial infection, and increased ICU stay in patients.[2,3] Even after acute care, the nutritional need is insufficient to supplement or consumption.[4,5]

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The screening tools like anthropometric measurements, functional assessment, physical examinations, history of patient dietary intake, and clinical diagnosis are mainly for hospitalized patients rather than ICU patients. Employing these screening tools are difficult in ICU setup as the patients are more severe, mechanically ventilated, sedated or less responsive.[6] Many of these requirements are difficult to meet in ICU patients because most of them require sedation and ventilatory support. Given the enormous volume necessary to maintain hemodynamic stability, weight swings might be influenced by fluid status.[3]

Inflammation is a contributing factor to hypermetabolism and muscle atrophy in critically ill patients. Understanding the patient's inflammatory condition is essential, but many standard approaches fall short of this goal. To address this issue, NUTRIC Score (NUTritional risk in Critically ill) was introduced. NUTRIC Score takes into account a patient's age, the number of comorbid conditions, sequential organ failure assessment (SOFA), acute physiology and chronic health evaluation (APACHE II), and interleukin 6 (IL-6).[7] In these individuals, this score approach highlights the nutritional risk linking malnutrition, inflammation, and outcome. Recent studies propose omitting measurement of IL-6 because it is not a frequently accessible test and applying modified modified Nutrition Risk in the Critically ill (mNUTRIC) as a tool for screening to assess nutritional risk.[8]

Many studies have evaluated the predictive accuracy of the mNUTRIC for mortality prediction. However, the results are inconsistent because the population is heterogeneous, the cut-off point is different, and the clinical context varies. In order for evidence-based use to be made in healthcare settings, it is necessary to calculate the pooled predictive power for mortality. The goal of the present meta-analysis is, therefore, to determine the pooled predictive value for mortality for the mNUTRIC.[9]

Materials and Methods

This meta-analysis followed the predefined protocol of this study and followed the guidelines of Preferred Reporting Items for the Systematic Review and Meta-Analysis (PRISMA). The protocol was registered in the PROSPERO (CRD42023460292).

Search Strategy for Identification of Studies

Literatures relevant to this meta-analysis were searched in the different databases such as PubMed, Web of Science, and Cochrane Library until 26 August 2023 using the search terms Modified NUTRIC or Modified NUTRIC score or mNUTRIC and mortality. To determine the mNUTRIC score for predicting mortality in patients admitted to the ICU, we reviewed retrospective or prospective cohort studies. Filters were used for literature published in English.

Selection Criteria for Included Studies

Two authors (Jay Prakash and Khushboo Saran) independently selected relevant references by evaluating title and abstracts preceding complete the study. If there were any differences, they were resolved through discussion, and if necessary, we consulted third authors (Archana Kumari). Throughout the paper review process, exclusion criteria were documented.

Inclusion and Exclusion Criteria

Inclusion criteria: Cohort studies (retrospective or prospective); Patients older than 18 years; studies that reported mortality and the mNUTRIC score with cut-off value.

Exclusion criteria: Review articles, abstract, presentations in conference, case reports, and case series that presented phenomenology without assessing outcomes and articles published other than English language.

Participants

Patients >18 years admitted in ICU

Exposure

Modified Nutrition Risk in the Critically ill score

Comparison

Cut-off value of mNUTRIC score mentioned individual study

Outcome

Mortality

Data Extraction and Quality Evaluation

On pre-made data abstraction forms, the two authors (Jay Prakash and Saket Verma) individually extracted data using a methodical approach. A two-tiered method was implemented to address any dispute. First, we let the authors to debate their concerns; but, if the problems persisted, we recommended that a third author (Archana Kumari) do independent data extraction before engaging in additional discussions to resolve the dispute.

The study features, data on demographics, results, and risk of bias for each study were gathered. We extracted mortality for 28 days as well as for various time periods. We collected data from every study that met the eligibility requirements such as authors, publication, country name, design of the study, sensitivity, specificity, number of survivors and non-survivors, and baseline and demographic parameters like sample size, age and sex of the patients, body mass index, comorbidities such as diabetes mellitus, hypertension, cardiac and respiratory disease, chronic kidney disease (CKD), infection, and coronavirus disease (COVID-19).

The risk of bias was assessed by Quality in Prognosis Studies (QUIPS) tool which provides an overview of the six bias domains, together with overall rating assessments.[10] The QUIPS tool ranks each of the following domains as "low," "moderate," or "high."

Statistical Analysis

We included all patients in our meta-analysis to predict mortality. The data were obtained by either by direct extraction or indirect calculation from the published literature. The study's weight was determined using DerSimonian and Laird random-effects models, as well as the inverse variance method. Study heterogeneity was evaluated by I^2 statistic and the Cochran Q test for heterogeneity.[11] In order to assess publication bias, we also examined the funnel plot visually.

We employed meta-regression analysis for looking into possible factors of study heterogeneity. The following variables were used as covariates or moderators in our analysis for potential sources of heterogeneity: continuous variable as mean age and cut-off value for mNUTRIC score as well as percentage of patients with diabetes and hypertension, male gender, patients with cardiac disease, respiratory disease, and chronic kidney disease.

We subsequently did a subgroup analysis based on cut-off value of mNUTRIC score <5 / >5, taking into consideration the clinical importance. In compliance with the guidelines of the Cochrane Collaboration, standard deviations (SD) were computed from

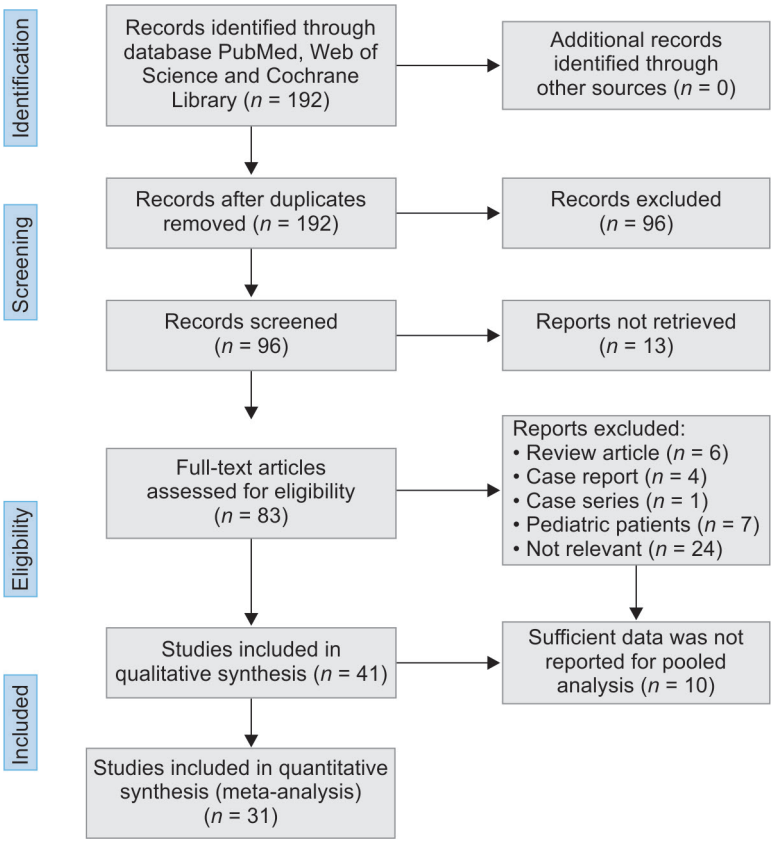

Fig. 1: PRISMA flow diagram

interquartile ranges (IQR), and a normal distribution was used for continuous data.[12] Finally, the results were displayed using forest plots. We used STATA version 13.0 (StataCorp. 2013. Stata Statistical Software: Release 13. College Station, TX: StataCorp LP) for statistical analyses. A *p*-value below 0.05 was deemed noteworthy.

Results

The Outcomes of Search and Study Characteristics

At first, 192 studies were determined to have qualifying potential. A total of 96 studies were screened after removing duplicates and titles and abstracts were examined (Fig. 1). We e-mailed the eight authors of the pertinent studies, but regrettably they did not reply. Ultimately, a pooled analysis of 31 cohort studies (retrospective and prospective), involving 13,271 participants, was used to assess the mNUTRIC score's ability to predict all-cause mortality.[3,13–43]

Table 1 displays the features of every included study that is a part of the current meta-analysis. Bias in the outcome measurement was low in 24 studies,[3,13–19,22–27,29–34,36,39–43] moderate in five studies,[20,28,35,37,38] and high risk of bias in two studies (Fig. 2).[21,39]

Outcomes

A total of 31,277 patients were included in the analysis from 31 studies meeting inclusion criteria. The summary area under the curve (sAUC) of 0.80 (95% CI: 0.76–0.83) (Fig. 3) illustrates the mNUTRIC score's strong discrimination. In predicting mortality in critically ill patients, the pooled sensitivity was 0.79 (95% CI: 0.74–0.84) and pooled specificity was 0.68 (95% CI: 0.63–0.73) (Fig. 4). A total of I^2 statistics showed a high value of heterogeneity/inconsistency (92% for sensitivity and 96% for specificity) (Fig. 4). The diagnostic odds ratio for predicting the mortality by mNUTRIC was 6 (95% CI: 6–15), and the positive likelihood ratios (PLR) and negative likelihood ratios (NLR) were 2 (95% CI: 2.0–3.2) and 0.3 (95% CI: 0.21–0.38), respectively (Fig. 5).

The funnel plot revealed no discernible publication bias ($p = 0.8$), which suggest validity of the study's observations (Fig. 6). When 50% was the pretest probability, the PLR was 2 and the posttest mortality was 71%. The NLR was 0.30, whereas the posttest negative predictive value was 23%. We looked at the clinically significant variables (mean age, male gender, BMI, hypertension, diabetes, cardiac disease, respiratory disease, chronic kidney disease, and infection) on the effect size to determine the source of heterogeneity, but with the exception of the cut-off value, which might help to explain the source of heterogeneity, we were unable to uncover any characteristics that could adequately explain the actual source of variation (Fig. 7).

Subgroup analysis was conducted based on cut-off value and we observed no discernible variation in the mNUTRIC's prediction accuracy between cut-off values of < 5 and > 5 and the sAUC were 0.82 (95% CI: 0.78–0.85) and 0.78 (95% CI: 0.74–0.81), respectively (Table 2).

We also did subgroup analysis based on 28 days mortality and others day. Our subgroup analysis demonstrated that the results were stable with respect to 28 days mortality (Table 2).

Discussion

The mNUTRIC is one of the most reliable indicators for predicting mortality among patients with critical illness. This meta-analysis, which uses a robust literature search, pre-registered methodology,

Table 1: Characteristics of the included studies

S.No	Author, Year	Country	Study design	Sample size	Cut-off	Sensitivity	Specificity	Survivor	Non-survivor	Mortality (Days)
1	Mukhopadhyay et al., 2017[13]	Singapore	Prospective observational cohort study	401	5	72	63	314	87	28
2	Wang et al., 2021[17]	China	Prospective observational cohort study	3107	4	61.48	78.81	2,567	540	28
3	Lin et al., 2021[21]	Taiwan	Retrospective observational study	205	>4	90.5	62.3	184	21	28
4	de Vries et al., 2018[27]	Netherlands	Retrospective cohort study	475	>4	88.4	48.9	354	121	28
5	Kalaiselvan 2017[36]	India	Prospective observational study	678	≥5	41.5	73.8	463	215	NA
6	Kumar et al., 2020[38]	India	Prospective cross-sectional study	1990	6	97.2	74	1,595	395	NA
7	Gulsoy et al., 2022[14]	Turkey	Prospective cohort study	311	4.5	0.88	0.736	182	129	28
8	Im et al., 2022[15]	Korea	Prospective observational cohort study	206	≥5	83.3	48.9	176	30	90
9	Jeong et al., 2018[16]	Korea	Retrospective cohort study	482	6	75	65	324	158	28
10	Kim et al., 2022[18]	Korea	Retrospective cohort study	220	≥5	81	44.4	162	58	NA
11	Mendes et al., 2017[3]	Portugal	Multicenter prospective cohort study	1122	≥5	73.25	58.4	879	243	NA
12	Dsouza et al., 2022[19]	India	Prospective observational study	250	>2	80.9	76.4	161	89	NA
13	Tsai et al., 2019[20]	Taiwan	Retrospective observational study	131	4.5	92	74.5	106	25	6 WK
14	Tseng et al., 2021[22]	Taiwan	Multicenter prospective cohort study	815	5.5	80	77.4	678	137	28
15	Alramly et al., 2020[23]	Jordan	Multicenter retrospective cohort study	737	4.5	67.9	54.8	85	652	30
16	Acehan et al., 2021[24]	Turkey	Retrospective observational study	125	4.5	73.5	63.2	81	44	NA
17	Mayr et al., 2020[26]	Germany	Retrospective observational study	114	≥6	78.3	71.1	45	69	90
18	Chen et al., 2023[28]	China	Retrospective study	234	≥3	100	42.6	216	18	28
19	Ata Ur-Rehman et al., 2018[29]	Pakistan	Prospective observational study	75	≥5	46.67	49.99	62	13	NA
20	Hai et al., 2022[30]	Vietnam	Prospective cross-sectional study	194	5	67.1	81	121	73	NA
21	Mahmoodpoor et al., 2023[31]	Iran	Prospective observational study	445	>4	92.11	94.1	407	38	NA
22	Brascher et al., 2020[42]	Brazil	Observational, longitudinal, prospective study	83	5	64.7	66.7	73	10	28
23	Todur et al., 2022[32]	India	Prospective observational study	216	≥4	82.1	65.9	138	78	NA
24	Zhang et al., 2022[33]	China	Retrospective observational study	268	≥5	82.5	81.7	199	69	NA
25	Wang et al., 2022[34]	China	Multicenter prospective observational study	1021	>4	76.45	56.63	694	327	28
26	Acehan et al., 2020[35]	Turkey	Prospective observational study	251	3.5	60	67.8	193	58	NA
27	Ma et al., 2022[37]	China	Retrospective cohort study	429	≥1	91.1	52.3	384	45	28
28	Zheng et al., 2021[25]	China	Retrospective cohort study	4059	4	75	63.98	3,967	92	NA
29	Kucuk et al., 2022[39]	Turkey	Retrospective study	322	>3.5	67.7	80	137	185	NA
30	Leoni et al., 2022[40]	Italy	Retrospective cohort study	98	5	75	89	53	45	28
31	Wełna et al., 2023[41]	Poland	Secondary analysis of prospective study	146	≥6	87.7	61.7	75	71	28

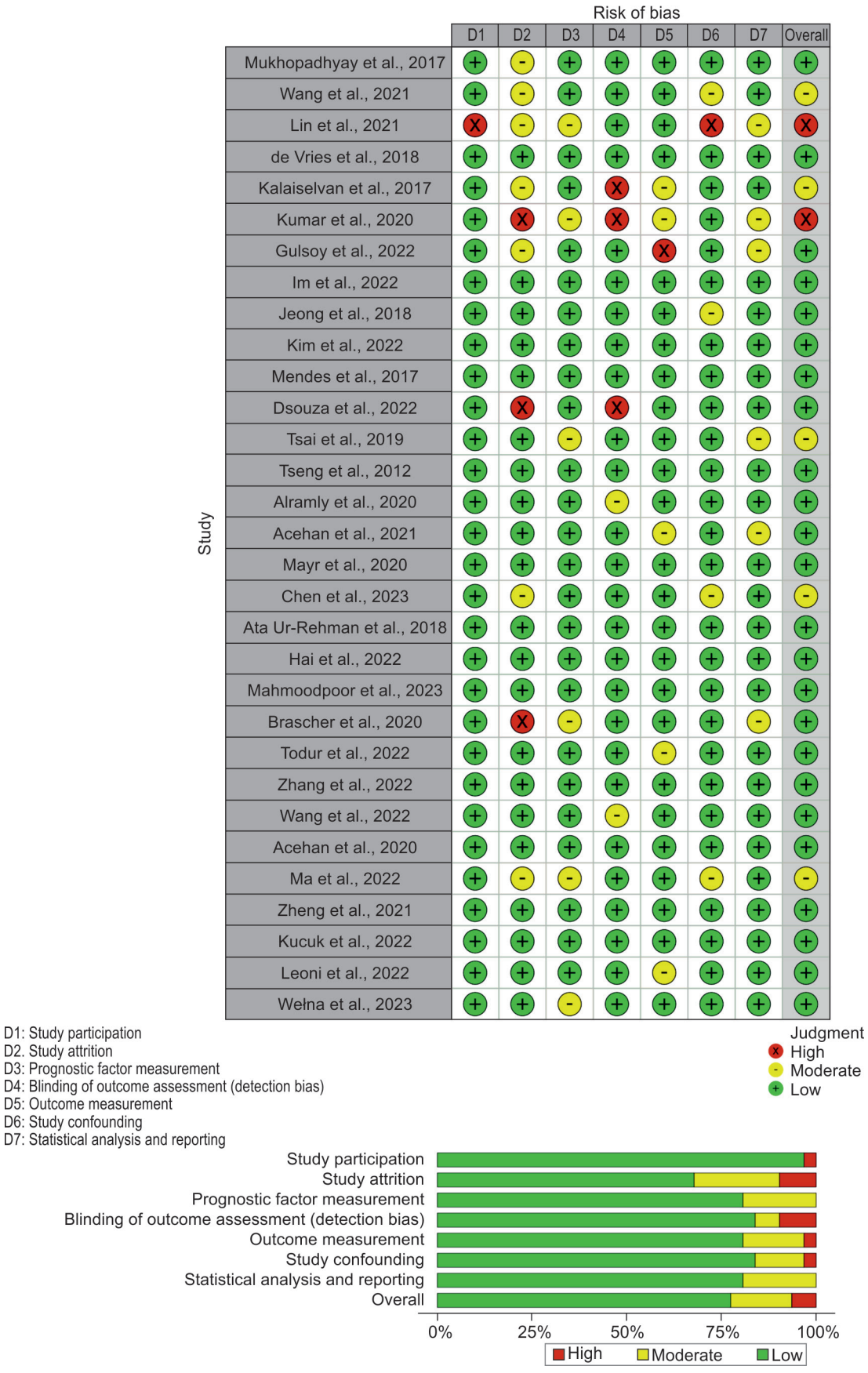

Fig. 2: Risk of bias summary

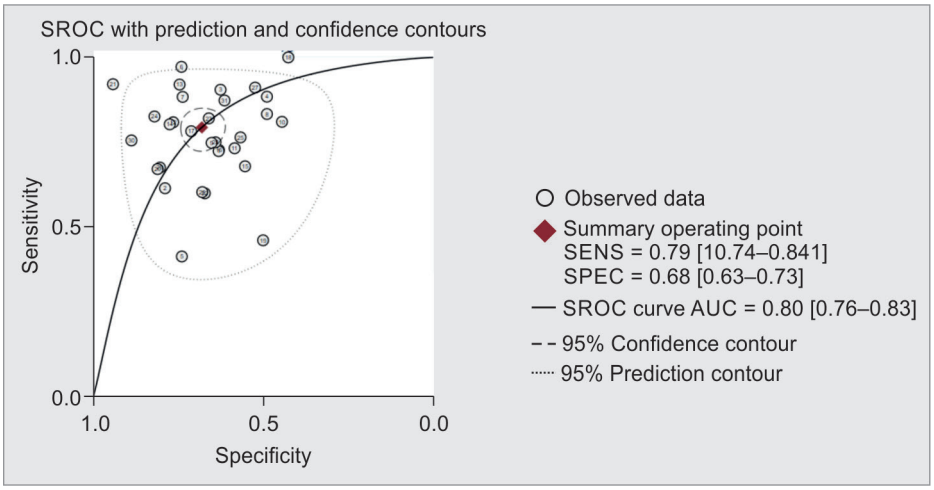

Fig. 3: Summary receiver operating characteristic graph for the included studies. The AUC of mNUTRIC for probability in predicting mortality was 0.80 (95% CI: 0.76–0.83)

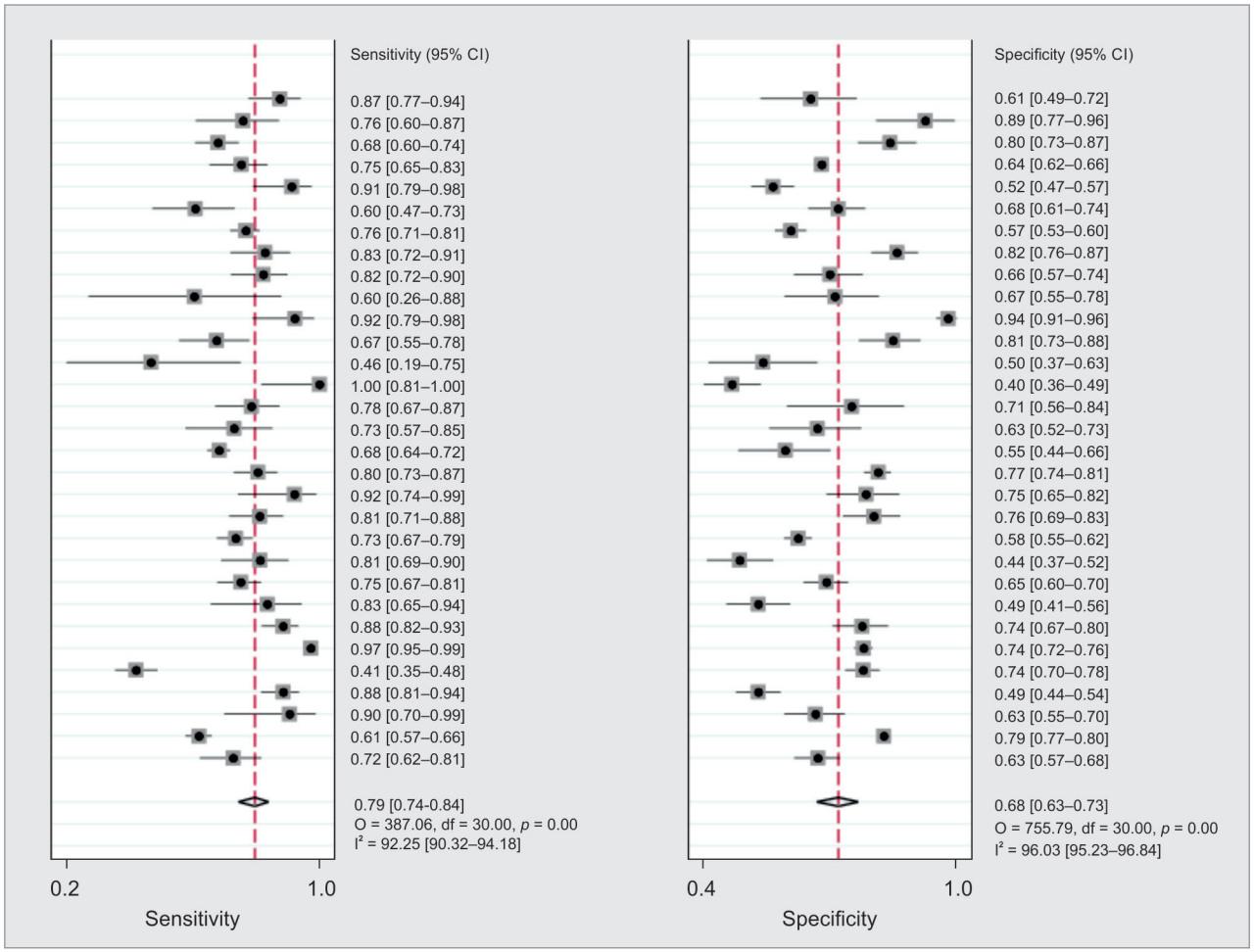

Fig. 4: Forest plot of the sensitivity and specificity of mNUTRIC for predicting mortality in critically ill patients. The pooled sensitivity and specificity were 0.79 (95% CI: 0.74–0.84) and 0.68 (95% CI: 0.63–0.73), respectively

the QUIPS tool for risk of bias analysis, and the inclusion of up to thirty-one existing studies, suggests that mNUTRIC has a strong ability to distinguish between critically ill patients and predict their mortality. This is the first mNUTRIC meta-analysis on all-cause mortality prediction in critically ill patients that we know of.

Because nutritional risk in the intensive care unit is linked to inflammation and a hypermetabolic state, most nutrition screening methods were ineffective before the mNUTRIC score was developed. These crucial factors were overlooked by the previous methods. In this context, a cutting-edge tool created specifically

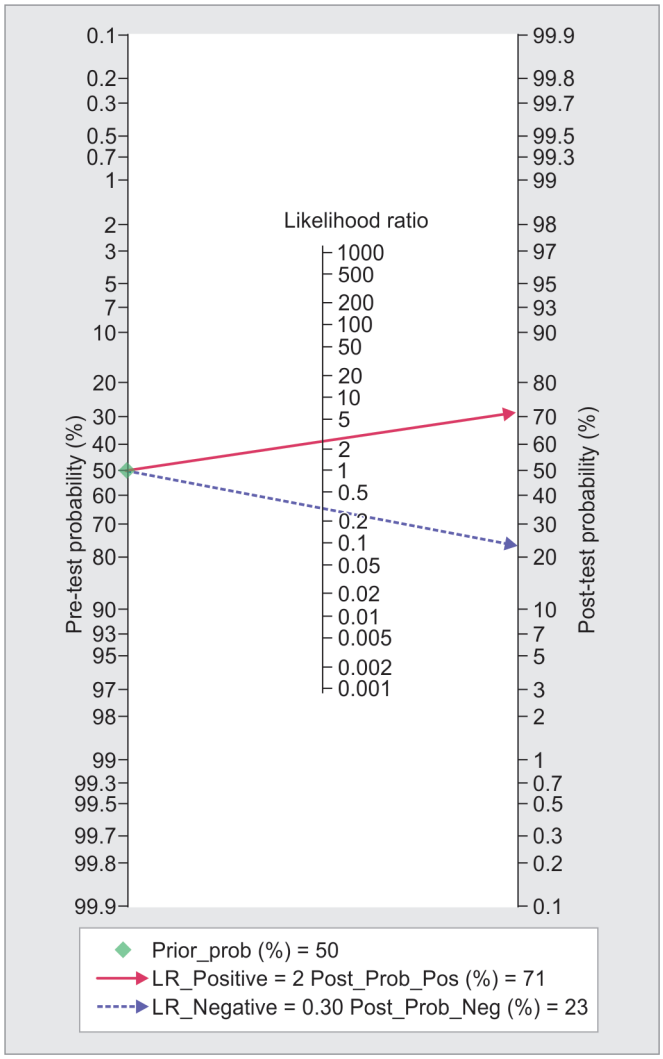

Fig. 5: Fagan nomogram showing pretest probability and posttest probability using mNUTRIC for predicting mortality

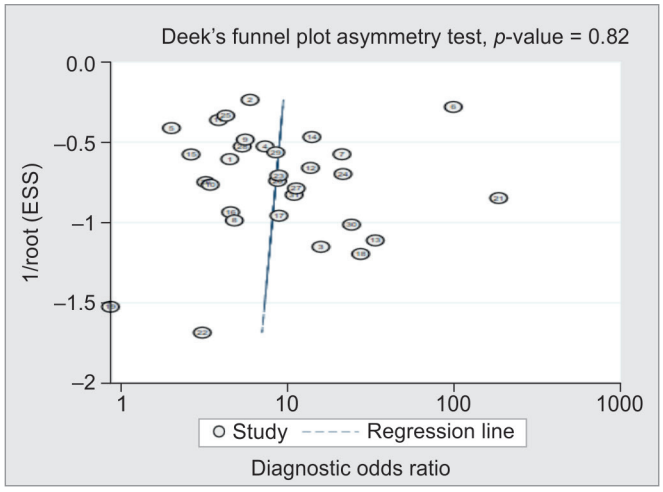

Fig. 6: Deek funnel plot showing publication bias for studies included in the meta-analysis

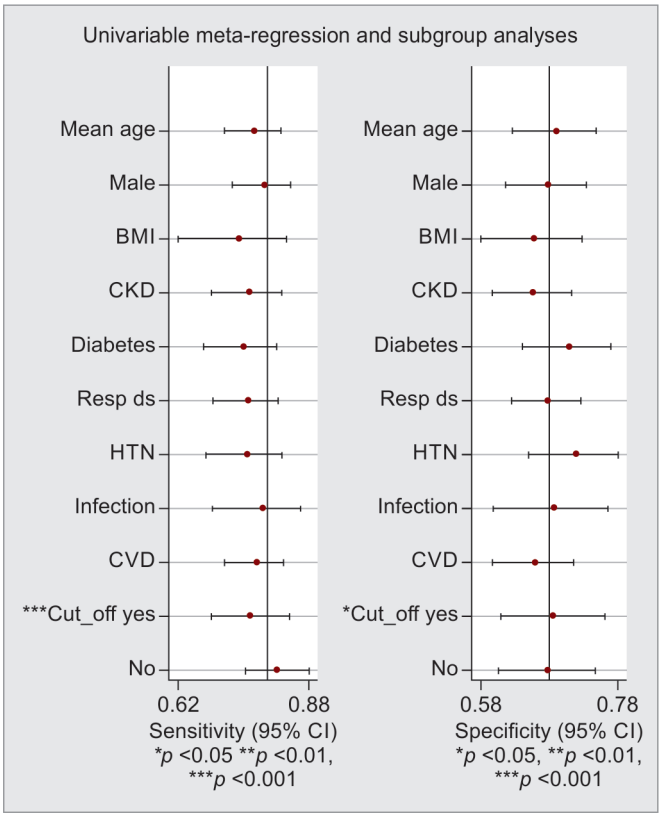

Fig. 7: Forest plot showing pooled sensitivity and pooled specificity of clinical variables for predicting mortality by mNUTRIC

for critically ill patients is the mNUTRIC score. The importance of the mNUTRIC score in predicting outcomes for critically ill patients has been demonstrated by numerous studies.[27,43] The effectiveness of the mNUTRIC score is limited in some ways like score might not identify patients who would benefit from supplementation (antioxidants, for example). The main emphasis of the score is on the supply of macronutrients, protein, and calories. The development of the NUTRIC score does not completely account for nutritional background and practices.

Several studies have reported varied mNUTRIC cut-off for predicting mortality. As a result, clinicians are unsure of the best mNUTRIC thresholds to use in order to predict outcomes. 28.2% of critically ill patients admitted to the intensive care unit (ICU) were found to be at high nutritional risk (mNUTRIC scores >5).[17] These results were in line with a previous study, where 22.4% of the patients were rated as having high scores (between 5 and 9).[44]

We found that risk stratification could be accomplished with the mNUTRIC score. In accordance to our meta-analysis, mNUTRIC may be able to distinguish between critically ill patients with a sAUC of 0.80 (95% CI: 0.76–0.83), sensitivity of 0.79 (95% CI: 0.74–0.84), and specificity of 0.68 (95% CI: 0.63–0.73). Inconsistency, or heterogeneity (I^2), was considerable (86% for sensitivity and 85% for specificity).

Using meta-regression analysis, we looked into the sources of variables that might affect variation in the studies. However, the presence of cardiac disease, respiratory conditions, chronic kidney disease, infection, BMI, and other possible clinical conditions did not explain the source of heterogeneity. Examples of such clinical

Table 2: Results of subgroup analysis using mNUTRIC score for predicting mortality

Categories	*Number of studies*	*Sensitivity (95% CI)*	*Specificity (95% CI)*	*sAUC (95% CI)*	*DOR (95% CI)*	*I2*
Cut-off score						
Cut-off <5	16	0.81 (0.75–0.86)	0.68 (0.60–0.75)	0.82 (0.78–0.85)	9 (6, 15)	Sensitivity: 88.01% Specificity: 97.27%
Cut-off ≥5	15	0.77 (0.68–0.84)	0.68 (0.61–0.74)	0.78 (0.74–0.81)	7 (14,–22)	Sensitivity: 94.61% Specificity: 93.81%
Mortality (28 days)						
Mortality (28 days)	13	0.82 (0.75–0.87)	0.65 (0.58–0.71)	0.80 (0.76–0.83)	8 (6, 12)	Sensitivity: 87.79% Specificity: 96.99%
Mortality (others day)	18	0.77 (0.79–0.84)	0.70 (0.63–0.76)	0.80 (0.76–0.83)	8 (4, 14)	Sensitivity: 94.42% Specificity: 95.40%

CI, confidence interval; DOR, diagnostic odds ratio; I^2, inconsistency; sAUC, summary area under the curve

conditions include the proportion of hypertension, diabetes, male gender, and mean age. Nonetheless, the cut-off value might be able to shed light on the source of heterogeneity and the absence of publication bias corroborated the findings of our meta-analysis.

The included studies used a variety of cut-off values, ranging from 2 to 6, to get a consistent and clinically acceptable cut-off. Early outcome prediction is essential in order to give patients the best care possible, and categorization in the early hours of life is necessary to predict mortality. Nevertheless, based on included studies that looked at the mNUTRIC, we observed after subgroup analysis that the mNUTRIC's discriminatory power was equal to what we looked at when all studies were taken into consideration.

Considering to the present meta-analysis's findings, the mNUTRIC may help to identify those who are more likely to experience poor outcomes.

Limitations

One of our study limitations was that the validity of the mNUTRIC score's prediction accuracy was limited because none of the studies that were part of the meta-analysis showed model calibration and validation. Additionally, as shown by I^2, we observe a significant degree of heterogeneity among the studies, underscoring the significance of carrying out well-planned prospective studies. The varying cut-off value of mNUTRIC may have resulted from differences in patient clinical settings. Furthermore, the inability to collect data from eight trials diminished the study's power.

Conclusion

Our meta-analysis showed that the mNUTRIC has a strong ability to discriminate between patients who are critically ill and predict their mortality. To support the current findings, more extensive multicenter studies at certain time intervals and with uniform cut-offs are required.

Acknowledgment

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