Nutritional risk in critically ill patients: how it is assessed, its prevalence and prognostic value: a systematic review

Aline Cattani, Igor C. Eckert, Júlia E. Brito, Rafaela F. Tartari, and Flávia M. Silva

Context: *Nutritional risk (NR) screening is the first step of nutrition care process. Few data are available in literature about its prevalence, nor, to our knowledge, is a universally accepted reference method for the intensive care unit (ICU).* ***Objective:*** *The aim for this systematic review was to summarize evidence regarding the prevalence of NR and the predictive validity of different tools applied for NR screening of critically ill patients.* ***Data Sources:*** *The PubMed, Embase, and Scopus databases were searched up to December 2019 using the subject headings related to critically ill patients and NR screening. The current systematic review is registered with PROSPERO (identifier: CRD42019129668).* ***Data Extraction:*** *Data on NR prevalence, predictive validity of nutritional screening tools, and interaction between caloric-protein balance and NR in outcome prediction were collected.* ***Data Analysis:*** *Results were summarized qualitatively in text and tables, considering the outcomes of interest.* ***Results:*** *From 15 669 articles initially identified, 36 fulfilled the inclusion criteria, providing data from 8 nutritional screening tools: modified Nutrition Risk in the Critically Ill (mNUTRIC; n = 26 studies) and Nutritional Risk Screening–2002 (NRS-2002; n = 7 studies) were the most frequent; the NR prevalence was 55.9% (range, 16.0% to 99.5%). Nutritional risk was a predictor of 28-day and ICU mortality in 8 studies. Interactions between caloric-protein balance and NR on outcome prediction presented were scarcely tested and presented heterogeneous results (n = 8).* ***Conclusions:*** *Prevalence of NR in patients in the ICU varies widely; a satisfactory predictive validity was observed, especially when mNUTRIC or NRS-2002 were applied.*

INTRODUCTION

According to the American Society for Parenteral and Enteral Nutrition (ASPEN), nutritional risk (NR) screening is a process of identifying patients who may be malnourished or at risk for malnutrition to determine if a detailed nutritional assessment and appropriate intervention are indicated.[1] According to the European Society for Clinical Nutrition and Metabolism (ESPEN), the purpose of nutritional screening is to evaluate the ability of nutritional factors in predicting clinical outcomes, considering disease-related metabolic demand.[2] This process should identify

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Key words: critical care, intensive care unit, nutrition assessment, nutritional risk.

doi: 10.1093/nutrit/nuaa031

patients with NR simply, provide rapid results, have high accuracy, and should be cost-effective.[3]

Nutritional risk screening is the first step of the nutrition care process and, according to ESPEN, a nutritional screening tool should answer the following 4 basic questions: (1) What is the patient's current nutritional condition? (2) Is the patient's nutritional condition stable? (3) Can the patient's nutritional condition can get worse? (4) Can the disease process accelerate nutrition deterioration? Body mass index, body weight loss, report of food-intake decrease, and disease metabolic demand are usually included in the screening tools to answer these questions, respectively.[4] There is international consensus that nutritional screening should be performed at hospital admission within the first 24–72 hours for all patients. The aim of screening is to reduce the incidence of malnutrition and its deleterious consequences.[5,6]

Several tools have been validated to screen hospitalized patients at NR.[7] In a Brazilian study conducted with 752 patients admitted at the Emergency Service, the Malnutrition Universal Screening Tool (MUST), Malnutrition Screening Tool, and Short Nutritional Assessment Questionnaire shared similar accuracy to the Nutritional Risk Screening–2002 (NRS-2002) in identifying risk of malnutrition, and all instruments were positively associated with long hospital stay, suggesting that in clinical practice, the 4 tools should be applied and the choice of 1 of them should be made considering the particularities of the service. In this study,[8] the prevalence of NR ranged from 29.3% to 37.1%, depending of the tool applied. In fact, several studies indicated patients with NR had worse clinical outcomes in terms of death and longer hospital stay.[9–11]

In critically ill patients, Heyland et al[12] proposed that NR should not be considered as the risk of malnutrition, because the inflammatory stress response and consequent protein catabolism put all critically ill patients at risk of malnutrition. Considering this aspect, the authors suggested NR in intensive care is the risk of adverse events that could be reduced by adequate nutritional therapy, and NR could be assessed by the Nutrition Risk in the Critically Ill (NUTRIC) score. This tool is composed of scores of severity, age, number of comorbidities, length of hospital stay before intensive care unit (ICU) admission, and interleukin-6 (IL-6) levels.[12] Because of the difficulty of obtaining IL-6 measurements in clinical practice, the NUTRIC Score was later validated without including IL-6; this is the modified NUTRIC (mNUTRIC).[13] A recent systematic review of 12 studies showed the mNUTRIC score is related to clinical outcomes in the ICU, and the prevalence of high scores reported from 9 studies ranged from 22.4% to 67.9%.[14] However, data about NR prevalence in the ICU setting assessed by other screening tools were not reviewed.

Disagreements are found in the literature about which methods should be used to identify NR in critically ill adults. ASPEN recommends determination of NR through NUTRIC or NRS-2002 (the latter was not developed for critically ill patients but it considers the severity of disease),[2,6] whereas ESPEN considers that every patient with an ICU length of stay (ICU LOS) longer than 48 hours should be considered as at NR, and they emphasize limitations of currently available tools for clinical practice.[15] In fact, until now, there has been no reference method universally accepted for NR screening in the ICU, which justifies compilation of data available in the literature. The information about the predictive validity of screening NR tools for use with critically ill patients could help define the best nutritional care process in the ICU.

Therefore, the aim of this systematic review was to summarize the evidence regarding the prevalence of NR and the predictive validity of different tools applied for NR screening in critically ill patients. The interaction between caloric-protein balance and NR in the outcome prediction also was reviewed.

METHODS

Design and registration

A systematic review of studies about NR in critically ill patients was conducted according to Cochrane Handbook recommendations and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses checklist.[16,17] The protocol of this study was registered with International Prospective Register of Systematic Reviews (identifier: CRD42019129668).

Search strategy and selection criteria

The research question of the current systematic review, constructed according to Participants, Exposure, Comparison, and Outcomes criteria (Table 1), was: What is the prevalence of nutritional risk in critically ill adult patients and what is the validity of different methods used for nutrition risk screening to predict clinical outcomes as mortality, mechanical ventilation (MV) duration and length of ICU stay?

The search for studies was performed in the PubMed, Embase, and Scopus databases, with no restrictions of language and date, using keywords for each database. The full electronic search strategy performed in PubMed is presented in **Box 1**. The list of articles was retrieved with date of publication from inception until March 20, 2019, and last updated on December 19, 2019. Abstracts published in annals of the ASPEN and ESPEN congresses from the last 5 years,

Table 1 **Participants, exposure, comparison, and outcomes criteria for inclusion of studies**

Parameter	Criteria
Participants	Critically ill adult patients
Exposure	Nutritional risk
Comparison	Patients with nutritional risk vs those without or with low nutritional risk
Outcomes	Death, mechanical ventilation duration, and length of intensive care unit stay

Box 1 **Full PubMed electronic search strategy**

"((((((((((((((((((((((((((((((Protein-Energy Malnutrition[Title/Abstract]) OR Malnutrition, Protein-Energy[Title/Abstract]) OR Malnutritions, Protein-Energy[Title/Abstract]) OR Protein Energy Malnutrition[Title/Abstract]) OR Protein-Calorie Malnutrition[Title/Abstract]) OR Malnutrition, Protein-Calorie[Title/Abstract]) OR Protein Calorie Malnutrition[Title/Abstract]) OR Malnutrition[Title/Abstract]) OR Undernutrition[Title/Abstract]) OR Nutritional Status[Title/Abstract]) OR Status, Nutritional[Title/Abstract]) OR Nutrition Status[Title/Abstract]) OR Status, Nutrition[Title/Abstract]) OR Nutrition Assessment[Title/Abstract]) OR Assessments, Nutrition[Title/Abstract]) OR Nutrition Assessments[Title/Abstract]) OR Nutritional Assessment[Title/Abstract]) OR Assessment, Nutritional[Title/Abstract]) OR Assessments, Nutritional[Title/Abstract]) OR Nutritional Assessments[Title/Abstract]) OR Assessment, Nutrition[Title/Abstract]) OR Nutritional risk[Title/Abstract]) OR Nutrition screening[Title/Abstract]) OR nutritional risk screening[Title/Abstract]) OR Nutrition Risk in the Critically Ill[Title/Abstract]) OR Modified NUTRIC Score[Title/Abstract]) OR NUTRIC[Title/Abstract]) OR Nutrition Risk Screening 2002[Title/Abstract]) OR NRS-2002[Title/Abstract]) OR Subjective Global Assesment[Title/Abstract])) AND ((((((((((((((((((Critical Care[Title/Abstract]) OR Care, Critical[Title/Abstract]) OR Intensive Care[Title/Abstract]) OR Care, Intensive[Title/Abstract]) OR Surgical Intensive Care[Title/Abstract]) OR Care, Surgical Intensive[Title/Abstract]) OR Intensive Care, Surgical[Title/Abstract]) OR Intensive Care Units[Title/Abstract]) OR Care Unit, Intensive[Title/Abstract]) OR Care Units, Intensive[Title/Abstract]) OR Intensive Care Unit[Title/Abstract]) OR Unit, Intensive Care[Title/Abstract]) OR Units, Intensive Care[Title/Abstract]) OR Critical Illnesses[Title/Abstract]) OR Illness, Critical[Title/Abstract]) OR Illnesses, Critical[Title/Abstract]) OR Critically Ill[Title/Abstract]) OR Critical Illness[Title/Abstract]) OR Critically Ill Patients[Title/Abstract])

as well as the reference lists of eligible studies, were manually screened.

Eligibility criteria

Studies were considered eligible if they reported data on the prevalence of NR and its association with clinical outcomes (ie, death, ICU LOS, MV duration) or data about the effect of nutritional intervention on outcomes according to the NR in critically ill patients (age $\geq$ 18 years). Editorials, reviews, and abstracts without full-text articles were excluded.

Process of study selection

The EndNote reference manager software program (version X7.17 [2011]; Thomas Reuters, New York, NY) was used to coordinate the review and track process. Two trained reviewers (A.C. and I.C.E.) independently screened the titles and abstracts, and subsequently evaluated the full-text versions of all potentially relevant articles. A third reviewer (F.M.S.) resolved all cases of disagreement.

Data extraction

Data extraction was performed in Google Forms (Google, Mountain View, CA) and exported to Microsoft Office Excel (Microsoft, Redmond, WA). It was guided by a standardized electronic form, independently performed by 3 reviewers grouped in 2 pairs (A.C. and I.C.E.; A.C. and J.E.B.). Disagreements were discussed, analyzed, and resolved through the arbitration of a fourth reviewer (F.M.S.). Characteristics extracted from each study included the first author's name, publication year, study location, study design, age and sex of participants, sample size, characteristics of ICU, severity of disease, NR screening tools and classification of risk, clinical outcomes (ie, ICU LOS, duration of MV, and death), and nutritional intervention prescribed and received. Authors were contacted in case of doubts regarding the study.

Assessment of study quality

The methodological quality of the studies was assessed by 3 reviewers grouped in 2 pairs (A.C. and I.C.E.; A.C. and J.E.B.) using the Newcastle Ottawa Scale (NOS) for cohort studies.[18] A fourth reviewer (F.M.S.) resolved cases of disagreement. The NOS evaluates 3 quality parameters (selection, comparability, and outcome) divided across 8 specific items, which slightly differ when scoring case-control and longitudinal studies. Each item on the scale was scored from 1 point, except comparability, which could be adapted to the specific topic of interest to score up to 2 points. Thus, the maximum score

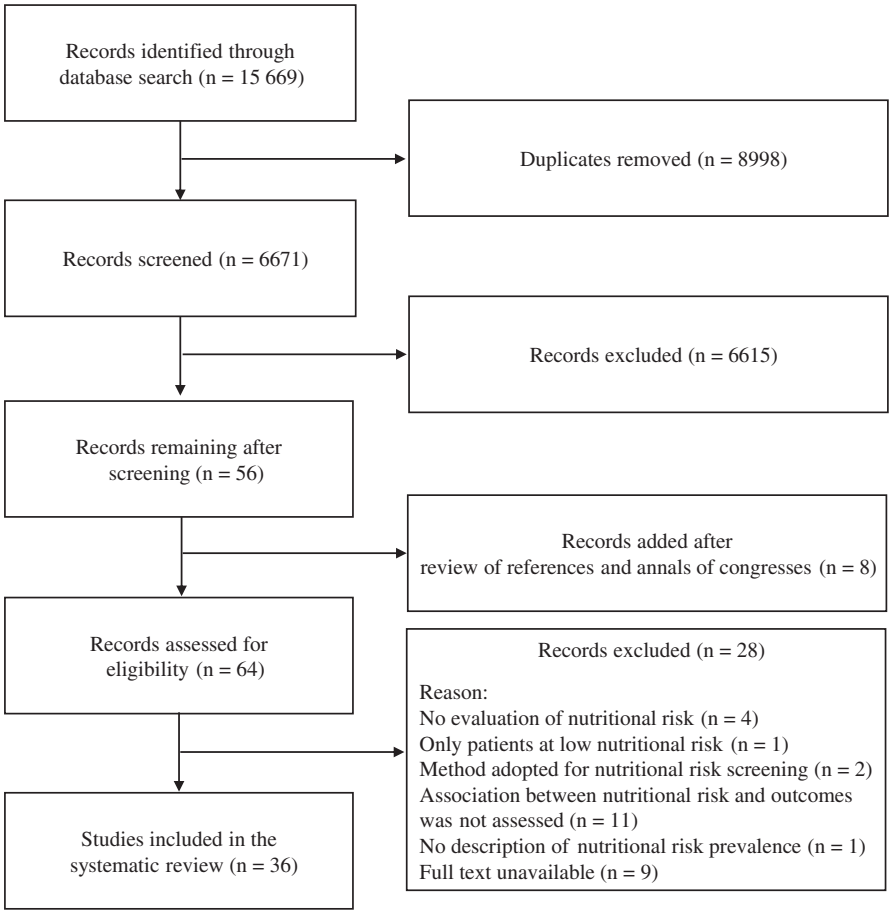

Figure 1: Study flow diagram.

for each study was 9, and studies having <7 points were identified as having a high risk of bias.[19]

Data synthesis

Results of eligible studies were summarized qualitatively in text and tables describing NR prevalence, predictive validity of nutritional screening tools, and interaction between caloric-protein balance and NR in outcome prediction. Prevalence data of NR were reported as the proportion of patients at NR as classified according to the specific tool used. Predictive validity was determined by bivariate analysis for outcome comparison (ie, ICU LOS, duration of MV, and 28-day ICU and hospital mortality rate) between patients with and those without or with low NR or results of multivariate analysis or area under the receiver operating characteristics curve (aROC).

A meta-analysis was not performed because studies used different screening tools and outcome measures, and patient characteristics differed in primary studies. Furthermore, most studies presented risk of bias.

RESULTS

Selection and general characteristics of included studies

A total of 15 669 articles were initially identified through database searches, of which 8998 were duplicates. Additional records through manual search and review of grey literature amounted to 8 articles. The full text of 64 studies was assessed for eligibility. The present systematic review included 36 studies addressing NR in critically ill patients (Figure 1).[12,13,20–53] The general features of eligible studies are presented in Table 2.

Regarding study designs, 25 were of prospective cohorts,[12,22–30,32–40,42,46,47,49–51,53] 8 were of retrospective cohorts,[20,21,31,41,43–45,48,52] and 1 was a post hoc analysis of a randomized clinical trial.[13] The studies included were conducted between 2008 and 2019 in 17 countries, most of them in Brazil (n = 6 studies)[22,32,49,51–53] and Singapore (n = 5 studies).[27–29,36,37] Of the 36 studies included, 19 were performed in mixed ICUs,[12,22,23,26–29,31,33–35,40,42,43,47,48,52,53] 8 in medical ICUs,[20,21,25,30,36,44,50,51] 3 in surgical ICUs,[38,41,45] and 1

Table 2 **Characteristics of studies about nutritional risk in critically ill patients**

Reference	Design; country	Sample					Tool	Predictive validity	Nutrition intervention interaction with nutritional risk
		No.	Age (years)[a]	Male Sex (%)	Severity disease score[a]	Type of ICU			
Ata ur-Rehman et al (2018)[30]	Prospective cohort; Pakistan	75	55.8 ± 25.0	53.4	APACHE II: 22.3 ± 9.5 SOFA: 8.2 ± 7.4	Medical	mNUTRIC	Yes, multivariate analysis Outcomes: ICU LOS, duration of MV, ICU mortality	No
Brascher et al. (2019)[51]	Prospective cohort ; Brazil	83	79.0 (63.0–86.0)	52.0	APACHE II: 16.0 (12.0–20.0) SOFA: 1.0 (0.0–3.0)	Medical	mNUTRIC	Yes, multivariate analysis Outcome: mortality[b]	No
Cândido et al (2019)[52]	Retrospective cohort; Brazil	82	63.1 ± 16.1	52.4	APACHE II: 14.7 ± 6.5 SOFA: 8.0 (1.0–17.0)	Mixed	mNUTRIC	Yes, bivariate analysis Outcomes: ICU LOS, ICU mortality	No
Chourdakis et al (2019)[46]	Prospective cohort; Greece	80	63.3 ± 15.6	63.7	APACHE II: 19.4 ± 8.2 SOFA: 7.9 ± 4.2	NR	mNUTRIC	Yes, bivariate analysis Outcomes: ICU LOS, duration of MV, 28-day mortality	No
Compher et al (2017)[47]	Secondary analyses of a prospective cohort; Canada and United States	2853	61.2 ± 17.3	60.9	APACHE: 22.5 ± 8.5 SOFA: 8.9 ± 3.7	Mixed	mNUTRIC	No	Yes
de Vries et al (2018)[48]	Retrospective cohort; Netherlands	475	71.5 (62.2–78.5)	56.6	APACHE II: 22.0 (17.5–27.5) SOFA: 8.0 (6.0–9.5)	Mixed	mNUTRICMUST	Yes, multivariate analysis Outcomes: duration of MV, 28-day mortality	No
Gonzalez et al (2019)[49]	Prospective cohort; Brazil	159	56.6 ± 20.0	51.0	APACHE II: 22.0 (5.0–26.0) SOFA: 6.0 (2.0–9.0)	NR	mNUTRIC	Yes, multivariate analysis Outcome: 28-day mortality	No
Hsu et al (2018)[50]	Prospective cohort; Taiwan	190	79.1 ± 7.2	56.8	APACHE 20–28: 43.2% SOFA 6–10: 43.7%	Medical	mNUTRIC	Yes, multivariate analysis Outcomes: ICU LOS, duration of MV, ICU mortality	No
Jeong et al (2019)[21]	Retrospective cohort; South Korea	248	68.0 (57.0–74.0)	69.8	APACHE: 22.0 (19.0–28.0) SOFA: 11.0 (8.0–14.0)	Medical	mNUTRIC	Yes, bivariate analysis Outcomes: ICU LOS, 28-day mortality	Yes
José et al (2019)[22]	Prospective cohort; Brazil	82	60.3 ± 18.5	61.0	NR	Mixed	mNUTRIC	Yes, multivariate analysis Outcome: mortality[b]	No
Kalaiselvan et al (2017)[23]	Prospective cohort; India	678	55.7 ± 17.5	67.6	APACHE II: 22.2 ± 7.3 SOFA: 6.7 ± 3.0	Mixed	mNUTRIC	Yes, multivariate analysis Outcomes: ICU LOS, duration of MV, mortality[b]	No
Lee et al (2018)[26]	Prospective cohort; Malaysia	155	51.3 ± 15.7	53.9	APACHE II: 26.9 ± 7.3 SOFA: 12.4 ± 3.7	General	mNUTRIC	No	Yes
Lew et al (2018)[27]	Prospective cohort; Singapore	439	61.4 ± 15.8	59.0	APACHE II: 24.5 ± 8.1 SOFA: 8.6 ± 3.8	Mixed	mNUTRIC	Yes, multivariate analysis Outcome: hospital mortality	No
Lew et al (2018)[28]	Prospective cohort; Singapore	252	59.8 ± 16.1	61.5	APACHE II: 26.0 (20.5–30.5) SOFA: 13.5 (7.0–10.5)	Mixed	mNUTRIC	No	Yes
Lew et al (2019)[29]	Prospective cohort; Singapore	440	61.4 ± 15.7	58.9	APACHE: 24.5 ± 8.1 SOFA: 8.7 ± 3.8	Mixed	mNUTRIC	Yes, bivariate analysis Outcome: 28-day mortality	No

(continued)

Table 2 **Continued**

Reference	Design; country	Sample					Tool	Predictive validity	Nutrition intervention interaction with nutritional risk
		No.	Age (years)[a]	Male Sex (%)	Severity disease score[a]	Type of ICU			
MacEachern et al (2019)[31]	Retrospective cohort; Canada	154	51.0 ± 16.0	44.0	APACHE II: 27.0 ± 8.0	Mixed	mNUTRIC	Yes, bivariate analysis Outcome: ICU LOS	No
Marchetti et al (2019)[53]	Prospective cohort; Brazil	200	59.4 ± 16.5	46.5	APACHE II: 14.7 ± 4.1 SOFA 5.0 (2.2–8.0)	Mixed	mNUTRICNRS-2002	Yes, multivariate analysis Outcomes: ICU LOS, hospital mortality	No
Mendes et al (2017)[33]	Prospective cohort; Portugal	1143	64.0 (51.0–75.0)	64.8	APACHE II: 20.0 (14.0–26.0) SOFA: 7.0 (5.0–10.0)	Mixed	mNUTRIC	Yes, multivariate analysis Outcomes: ICU LOS, duration of MV, 28-day mortality	No
Moretti et al (2014)[34]	Prospective cohort; Argentina	368	52.0 (18.0–93.0)	68.0	APACHE II: 20.7 ± 7.8 SOFA: 7.7 ± 3.5 SAPS: 52.8 ± 19.5	Mixed	mNUTRICNUTRI-C-CRP	Yes, multivariate analysis Outcomes: duration of MV, ICU mortality	No
Mukhopadhyay et al (2017)[36]	Prospective cohort; Singapore	401	60.0 ± 16.3	62	APACHE II: 27.3 ± 8.0 SOFA: 8.7 ± 3.8	Medical	mNUTRIC	Yes, multivariate analysis Outcomes: ICU LOS, duration of MV, 28-day mortality	Yes
Mukhopadhyay et al (2018)[37]	Prospective cohort; Singapore	48	66.0 (55.0–72.5)	71	APACHE II: 31.0 (25.0–34.0) CCI: 4.0 (1.5–6.0)	NR	mNUTRIC	Yes, bivariate analysis Outcomes: ICU LOS, duration of MV, 28-day mortality	No
Rahman et al (2016)[13]	Post hoc analysis of a randomized control trial; Canada	1199	50–75 years: 59.2%	NR	APACHE 20–28: 42.4% SOFA 6 to < 10: 52.0%	NR	mNUTRIC	Yes, multivariate analysis Outcome: 28-day mortality	Yes
Tsai et al (2019)[43]	Retrospective cohort; Taiwan	131	54.5 ± 14.2	83.2	APACHE: 20.6 ± 8.3 SOFA: 7.6 ± 3.5	Mixed	mNUTRIC	Yes, multivariate analysis Outcomes: ICU LOS, 6-week mortality	No
Wang et al (2018)[44]	Retrospective cohort; Taiwan	742	67.8 ± 16.2	66.6	APACHE II: 26.9 ± 6.8	Medical	mNUTRIC	Yes, bivariate analysis Outcomes: duration of MV, ICU LOS, 28-day mortality	Yes
Heyland et al (2011)[12]	Prospective cohort; Canada	597	63.9 (51.7–73.3)	58.2	APACHE: 21.0 (16.0–27.0) SOFA: 7.0 (5.0–9.0)	Mixed	NUTRIC	Yes, multivariate analysis Outcome: 28-day mortality	Yes
Jeong et al (2018)[20]	Retrospective cohort; South Korea	482	66.0 (56.0–74.0)	68.0	APACHE II: 21.0 (16.0–28.0) SOFA: 10.0 (7.0–14.0)	Medical	NUTRICmNUTRIC	Yes, multivariate analysis Outcomes: ICU LOS, 28-day mortality	No
Moretti et al (2018)[35]	Prospective cohort; Argentina	69	42.7 ± 17.0	72.56	SOFA: 6.5 ± 3.3 APACHE II: 16.7 ± 6.7 SAPS: 40.1 ± 15.3	Mixed	NUTRIC-CRP	Yes, bivariate analysis Outcomes: duration of MV, ICU mortality	No
Auiwattanakul et al (2019)[41]	Retrospective cohort; Thailand	1503	65.0 ± 4.0	57.2	APACHE II: 15.5 (12.0–21.0)	Surgical	NRS-2002	Yes, multivariate analysis Outcome: 28-day mortality	No
Köseoğlu et al (2011)[24]	Prospective cohort; Turkey	100	32.9 ± 12.4	NR	APACHE II: 6.5 ± 5.0	Trauma	NRS-2002	Yes, multivariate analysis Outcomes: ICU LOS, mortality*	No

(continued)

Table 2 **Continued**

Reference	Design; country	Sample					Tool	Predictive validity	Nutrition intervention interaction with nutritional risk
		No.	Age (years)[a]	Male Sex (%)	Severity disease score[a]	Type of ICU			
Küçükardali et al (2008)[25]	Prospective cohort; Turkey	342	67.0 ± 21.8	NR	APACHE II: 18.6 ± 3.9	Medical	NRS-2002	Yes, bivariate analysis Outcomes: ICU LOS, mortality[b]	No
Maciel et al (2019)[32]	Prospective cohort; Brazil	184	58.6 ± 15.4	48.9	SAPS: 57.3 ± 14.2 SOFA: 5.9 ± 3.5	Mixed	NRS-2002	Yes, multivariate analysis Outcomes: ICU LOS, duration of MV, ICU mortality	No
Özbilgin et al (2016)[38]	Prospective cohort; Turkey	152	67.1 ± 16.3	NR	APACHE: 13.5 ± 5.0 SOFA: 3.1 ± 2.1 CCI: 5.7 ± 3.1	Surgical	NRS-2002 MNA-SF mNUTRIC	Yes, multivariate analysis Outcomes: ICU LOS, duration of MV	No
Shpata et al (2015)[40]	Prospective cohort; Albania	963	60.8 ± 16.2	56.9	APACHE II 17.2 ± 5.5	Mixed	NRS-2002	Yes, multivariate analysis Outcomes: ICU LO, ICU mortality	No
Chittawatanarat et al (2016)[45]	Retrospective cohort; Thailand	1685	66.6 (53.4–76.9)	56.9	APACHE II: 13.2 (9.1–18.2)	Surgical	BNT/NT	Yes, multivariate analysis Outcome: 28-day mortality	No
Tripathy et al (2014)[42]	Prospective cohort; India	109	74.7 ± 8.4	73.4	APACHE II: 19.2 ±6.5	Mixed	MUST	Yes, multivariate analysis Outcome: 28-day mortality	No
Ramírez et al (2008)[39]	Prospective cohort; Colombia	228	48.8 ± 21.5	48.2	NR	NR	NSR	Yes, multivariate analysis Outcome: mortality[b]	No

aData reported as ±standard deviation or in parentheses as a range.

bUnspecified.

Abbreviations: APACHE II, Acute Physiology and Chronic Health Evaluation II; BNT/NT, Bhumibol Nutrition Triage/Nutrition Triage; CCI, Charlson Comorbidity Index; CRP, C-reactive protein; ICU, intensive care unit; LOS, length of stay; MUST, Malnutrition Universal Screening Tool, MV, mechanical ventilation, MNA-SF, Mini Nutritional Assessment; mNUTRIC, modified Nutrition Risk in the Critically Ill score; NR, not reported; NRS-2002, Nutritional Risk Screening; NSR, Nutritional Score Risk; NUTRIC, Nutrition Risk in the Critically Ill; SAPS, Simplified Acute Physiology Score; SOFA, Sepsis-Related Organ Failure Assessment.

in a trauma ICU.[24] Five studies did not provide this information.[13,37,39,46,49]

The mean number of patients included for eligible studies was 474.8 (range, 48[37] to 2853[47]). The mean age of patients was 61.0 years (range, 32.9[24] to 79.1[50] years) and the proportion of male patients was 59.9% (range, 44.0%[31] to 83.2%[43]). To quantify severity of patient illness, 31 studies[12,20,21,23–31,33–38,40–49,51–53] used the Acute Physiology and Chronic Health Evaluation II (APACHE II) and the average score was 20.5 (range, 6.5[24] to 31.0[37]), and 23 studies[12,20,21,23,26–30,32–36,38,43,46–49,51–53] used the Sepsis-Related Organ Failure Assessment (SOFA) tool, with an average score of 7.7 (range, 1.0[51] to 13.5[28]).

Eight NR screening tools were evaluated in the eligible studies in this systematic review. The most frequently used tools were mNUTRIC (n = 26 studies)[13,20–23,26–31,33,34,36–38,43,44,46–53] and NRS-2002 (n = 7 studies).[24,25,32,38,40,41,53] The components of nutritional screening tools with a frequency of ≥2 studies and the respective cutoff points for risk classification are described in Table 3. Predictive validity assessment was described in all included studies. The outcomes of death, MV duration, and ICU LOS were evaluated in 30,[12,13,20–25,27,29,30,32–37,39–46,48–53] 8,[23,30,32–38,44,46,48,50] and 19 studies,[20,21,23–25,30–33,36–38,40,43,44,46,50,52,53] respectively. Eight studies evaluated if a nutritional intervention modified the association between NR and clinical outcomes.[12,13,21,26,28,36,44,47]

Quality assessment

The detailed description of risk of bias in individual studies assessed by NOS is presented in Table 4. The mean score was equal to 6 points (range, 4[31] to 7[22,27,32,33,36,40,42,45,47,50,53]), and most of the studies (69.4%) presented high risk of bias (NOS score < 7).[12,13,19,20,22–25,27–30,33,34,36–38,40,42,43,45,47,48,51,52] Regarding the component selection, only 1 study received the maximum points[33]; most studies received 3 points (77.8%).[12,13,22–30,32,34–42,45–47,49–51,53] For the comparability criteria, the majority of studies (66.7%) received no points,[12,13,20,21,23–26,28–31,33–39,44,46,48,49,51,52] whereas in the component outcome, 30 studies (88.9%) received 3 points.[12,13,20–24,26–30,32–40,42–50,52,53]

Nutritional risk prevalence

The mean prevalence of NR in critically ill patients was 55.9% (range, 16.0%[35] to 99.5%[32]). These data were reported by 33 of the 36 eligible studies. The prevalence of NR reported among studies using any version of NUTRIC ranged from 16.0%[34] to 91.1%.[50] Considering studies reporting NR identified by NRS-2002, prevalence ranged from 39.4%[25] to 99.5%.[32] According to other screening tools applied, the prevalence of NR ranged from 47.7%[42] to 94.7%.[38]

When considering studies conducted in surgical ICUs, the mean prevalence of NR was 59.1% (range, 22.4%[38] to 94.7%[38]), whereas in clinical ICU, the mean was 60.7% (range, 27.7%[51] to 91.1%[50]). In mixed ICUs, the mean prevalence of NR was 51.0% (range, 16.0[35] to 99.5%[32]).

Predictive validity of nutritional screening tools

Different statistical methods were applied to evaluate the association between NR and clinical outcomes in the studies included in this review. Detailed information on clinical outcomes evaluated by the included studies is reported in Table 5.

Of 31 studies in which mortality was evaluated as an outcome, 15 reported 28-day mortality data,[12,13,20,21,27,33,36,37,41,42,44–46,48,49] 7 reported ICU mortality data,[30,32,34,35,40,50,52] 6 studies did not specify,[22–25,39,51] and 3 studies reported 6-week mortality[43] and hospital mortality data.[27,53] Bivariate analysis was performed in 20 studies, and a significant difference of death incidence between patients with NR and those without or with low NR was demonstrated in 16 studies.[20,23,24,26,27,31,33,34,36,37,41–43,46,53] ICU mortality and 28-day mortality were significantly associated with NR in 3[33,36,52] of 4 studies and in 7[31,34,37,41–43,46] of 9 studies, respectively. Fourteen studies used aROC curve construction to test the predictive validity of NR for death and a satisfactory accuracy (> 75%) to predict 28-day mortality was observed in 4.[12,20,48,49] Studies using aROC curve construction and reporting ICU[30,34] and hospital[27] deaths did not demonstrate satisfactory accuracy to predict death. Finally, by multivariate analysis, NR was a predictor of 28-day mortality in 5[20,33,36,45,49] of 6 studies, and the risk for death ranged from 1.48[36] to 4.04[45] in patients with NR in comparison with patients without or with low NR. Four studies[32,40,45,50] demonstrated that NR was also a predictor of ICU mortality; the risk of death ranged from 1.71[50] to 3.77.[45] Studies reporting hospital,[27,53] 6-week,[43] and unspecified[22] mortality data demonstrated a risk of death ranging from 2.34[53] to 33.65[43] in patients with NR in comparison with patients without NR.

All studies using NUTRIC (n = 2)[12,20] demonstrated accuracy in predicting death, considering an aROC curve > 75%, whereas 4[20,48,49,51] of 11 studies using mNUTRIC had satisfactory level of accuracy to predict death. The others tools for which accuracy in predicting mortality was assessed were NRS-2002,[24] MUST,[48] NUTRIC-CRP,[34] and Nutritional Score Risk (NSR),[39] and the results were not clinically relevant (aROC curve < 0.75). Multivariate analysis by

Table 3 **Components of the different screening tools applied at least twice in the eligible studies to identify patients at nutritional risk**

Characteristic	NUTRIC	mNUTRIC	NUTRIC-CRP	NRS-2002	MUST
Age	X	X	X	X	
APACHE II	X	X	X		
SOFA	X	X	X		
Comorbidities	X	X	X		
Days from hospital to ICU admission	X	X	X		
IL-6	X				
CRP			X		
BMI				X	X
Percentage of weight loss				X	X
Energy intake compared with energy requirement				X	
Severity of disease				X	X
Energy delivery before ICU admission					X
Nutrition risk classification	$\leq$ 5: Low risk $\geq$ 6: High risk	$\leq$ 4: Low risk $\geq$ 5: High risk	$\leq$ 5: Low risk $\geq$ 6: High risk	$<$ 3: No risk $\geq$ 3: Risk $\geq$ 5: High risk	0: Low risk 1: Medium risk $\geq$ 2: High risk
No. of studies using the tool	2	26	2	7	2

Abbreviations: APACHE II, Acute Physiology and Chronic Health Evaluation II; BMI, body mass index; CRP, C-reactive protein; ICU, intensive care unit; IL-6, interleukin-6, MUST, Malnutrition Universal Screening Tool; mNUTRIC, modified Nutrition Risk in the Critically Ill Score; NUTRIC, Nutrition Risk in the Critically Ill; NRS-2002, Nutritional Risk Screening; SOFA, Sepsis-Related Organ Failure Assessment.

Table 4 **Quality assessment of primary studies**

Reference	Selection (points)	Comparability (points)	Outcome (points)	Total score (out of 9 points)
Ata ur-Rehman et al (2018)[30]	3	0	3	6/9
Auiwattanakul et al (2019)[41]	3	1	2	6/9
Brascher et al (2019)[51]	3	0	2	5/9
Cândido et al (2019)[52]	2	0	3	5/9
Chittawatanarat et al (2016)[45]	3	1	3	7/9
Chourdakis et al (2019)[46]	3	0	3	6/9
Compher et al (2017)[47]	3	1	3	7/9
de Vries et al (2018)[48]	2	0	3	5/9
Gonzalez et al (2019)[49]	3	0	3	6/9
Heyland et al (2011)[12]	3	0	3	6/9
Hsu et al (2018)[50]	3	1	3	7/9
Jeong et al (2018)[20]	2	0	3	5/9
Jeong et al (2019)[21]	2	0	3	5/9
José et al (2019)[22]	3	1	3	7/9
Kalaiselvan et al (2017)[23]	3	0	3	6/9
Köseoğlu et al (2011)[24]	3	0	3	6/9
Küçükardali et al (2008)[25]	3	0	2	5/9
Lee et al (2018)[26]	3	0	3	6/9
Lew et al (2018)[27]	3	1	3	7/9
Lew et al (2018)[28]	3	0	3	6/9
Lew et al (2019)[29]	3	0	3	6/9
MacEachern et al (2019)[31]	2	0	2	4/9
Maciel et al (2019)[32]	3	1	3	7/9
Marchetti et al (2019)[53]	3	1	3	7/9
Mendes et al (2017)[33]	4	0	3	7/9
Moretti et al (2014)[34]	3	0	3	6/9
Moretti et al (2018)[35]	3	0	3	6/9
Mukhopadhyay et al (2017)[36]	3	1	3	7/9
Mukhopadhyay et al (2018)[37]	3	0	3	6/9
Özbilgin et al (2016)[38]	3	0	3	6/9
Rahman et al (2016)[13]	3	0	3	6/9
Ramírez et al (2008)[39]	3	0	3	6/9
Shpata et al (2015)[40]	3	1	3	7/9
Tripathy et al (2014)[42]	3	1	3	7/9
Tsai et al (2019)[43]	2	1	3	6/9
Wang et al (2018)[44]	2	0	3	5/9

Table 5 **Nutritional risk prevalence, predictive validity of nutritional risk screening tools, and interaction with nutrition intervention in outcomes prediction**

Reference	Tool	Nutritional risk prevalence (%)	Predictive validity			Nutrition intervention, risk score, and outcomes interaction
			ICU LOS	Duration of MV	28-day mortality	
Ata ur-Rehman et al (2018)[30]	mNUTRIC	High risk: 60.0	Low risk: 3.5 ± 4.0 High risk: 11.5 ± 5.0*	Low risk: 1.2 ± 2.0 High risk: 5.0 ± 2.0*	NR	NR
Brascher et al (2019)[51]	mNUTRIC	High risk: 27.7	NR	NR	aROC: 0.79 (95%CI: 0.67–0.89)	NR
Cândido et al (2019)[52]	mNUTRIC	High risk: 43.9	Low risk: 3.0 (1.0–50.0) High risk: 7.0 (1.0–91.0)*	NR	Low risk: 31.6% High risk: 68.4%*	NR
Chourdakis et al (2019)[46]	mNUTRIC	High risk: 56.2	Low risk: 4.0 (2.0-19.0) High risk: 9.0 (5.0-16.0)	Low risk: 4.0 (1.0–17.0) High risk: 9.0 (3.0–14.0)	Low risk: 17.1% High risk: 40.0%*	NR
Compher et al (2017)[47]	mNUTRIC	NR	NR	NR	NR	High-risk: negative interaction in 4 days; positive interaction in 12 days Low-risk: no interaction
de Vries et al (2018)[48]	mNUTRIC	High risk: 60.6	NR	aROC for > 2-day MV: 0.666 (95%CI 0.616–0.716)	aROC: 0.768 (95%CI, 0.722–0.814)	NR
	MUST	NR	NR	aROC for > 2-day MV: 0.532 (95%CI 0.469–0.594)	aROC: 0.513 (95%CI, 0.445–0.587)	NR
Gonzalez et al (2019)[49]	mNUTRIC	NR	NR	NR	aROC: 0.791 (95%CI, 0.7–0.9) RR: 2.97* (95%CI, NR)	NR
Hsu et al (2018)[50]	mNUTRIC	High risk: 91.1	OR: 1.18* (95%CI, NR)	OR: 1.52* (95%CI NR)	NR	NR
Jeong et al (2019)[21]	mNUTRIC	High risk: 88.7	Low risk: 11.0 (9.0–19.0) High risk: 14.0 (9.0–25.0)	NR	Low risk: 17.9% High risk: 36.4%	High-risk: positive interaction Low-risk: no interaction
José et al (2019)[22]	mNUTRIC	High risk: 48.8	NR	NR	NR	NR
Kalaiselvan et al (2017)[23]	mNUTRIC	High risk: 42.5	Low risk: 7.8 ± 5.8 High risk: 9.0 ± 4.2*	Ventilator-free days Low risk: 2.0 ± 2.8 High risk: 1.7 ± 1.9	NR	NR
Lee et al (2018)[26]	mNUTRIC	High risk: 55.8	NR	NR	NR	High risk: no interaction Low risk: negative interaction
Lew et al (2018)[27]	mNUTRIC	High risk: 67.9	Low risk: 2.0 (1.0, 4.0) High risk: 2.0 (1.0, 4.0)	Low risk: 2.0 (1.0, 3.0) vs High risk: 2.0 (1.0, 4.0)	NR	NR
Lew et al (2018)[28]	mNUTRIC	High risk: 54.3	NR	NR	NR	High risk: no interaction Low risk: no interaction
Lew et al (2019)[29]	mNUTRIC	High risk: 68.0	NR	NR	Low risk: 8.9%High risk: 91.1%*	NR
Maceachern et al (2019)[31]	mNUTRIC	High risk: 78.0	Low risk: 5.0 High risk: 10.0*	NR	NR	NR

(continued)

Table 5 **Continued**

Reference	Tool	Nutritional risk prevalence (%)	Predictive validity			Nutrition intervention, risk score, and outcomes interaction
			ICU LOS	Duration of MV	28-day mortality	
Marchetti et al (2019)[53]	mNUTRIC	High risk: 36.5	Low risk: 4.0 (2.0–8.0) High risk: 5.0 (8.0–8.5)	NR	RR: 3.48 (95%CI, 1.88–6.44)	NR
	NRS-2002	High risk: 55.0	Low risk: 3.0 (0.0–8.0) High risk: 5.0 (0.0–8.0)*	NR	RR: 1.86 (95%CI, 1.01–3.41)	NR
Mendes et al (2017)[33]	mNUTRIC	High risk: 48.6	OR LOS $\geq$ 9 days: 1.72 (95%CI, 1.36–2.17)	OR for ventilator-free days: 1.46 (95%CI, 1.16–1.85)	aROC: 0.658 (95%CI, 0.620–0.696) OR: 3.84 (95%CI, 2.84–5.26)	NR
Moretti et al (2014)[34]	mNUTRIC	High risk: 34.8	NR	Correlation in survivors group: 0.162*	NR	NR
	NUTRIC-CRP	High risk: 25.0	NR	Correlation in survivors group: 0.195*	NR	NR
Mukhopadhyay et al (2017)[36]	mNUTRIC	High risk: 45.4	Low risk: 3.5 (2.0–7.0) High risk: 5.0 (3.0–9.0)*	Low risk: 2.1 (1.2–3.7) High risk: 3.3 (1.5–5.7)*	aROC: 0.71 (95%CI, NR) OR: 1.48 (95%CI, 1.25–1.74)	High risk: negative interaction Low risk: no interaction
Mukhopadhyay et al (2018)[37]	mNUTRIC	High risk: 72.9	Low risk: 4.0 (3.0–5.0) High risk: 7.0 (3.0–11.0)*	Low risk: 3.0 (2.0–4.0) High risk: 5.0 (3.0–9.0)*	Low risk: 7.7% High risk: 28.6%	NR
Rahman et al (2016)[13]	mNUTRIC	NR	NR	NR	aROC: 0.648 (95%CI, NR)	High risk: positive interaction
Tsai et al (2019)[43]	mNUTRIC	High risk: 38.2	Low risk: 6.1 $\pm$ 6.3 High risk: 11.2 $\pm$ 10.6*	NR	NR	NR
Wang et al (2018)[44]	mNUTRIC	High risk: 75.3	Low risk: 13.2 $\pm$ 13.7 High risk: 16.7 $\pm$ 15.1*	Low risk: 11.4 $\pm$ 7.3 High risk: 13.9 $\pm$ 8.3*	Low risk: 14.2% High risk: 24.5%	High risk: positive interaction Low risk: No interaction
Heyland et al (2011)[12]	NUTRIC	High risk: 36.6	NR	NR	aROC: 0.783 (95%CI, NR)	High risk: positive interaction Low-risk: no interaction
Jeong et al (2018)[20]	NUTRIC	High risk: 52.9	Low risk: 5.0 (3.0–9.0) High risk: 9.0 (4.0–17.0)*	NR	aROC: 0.762 (95%CI, 0.718–0.806)	NR
	mNUTRIC	High risk: 65.6	Low risk: 5.0 (3.0–9.0) High risk: 8.0 (4.0–17.0)*	NR	aROC: 0.757 (95%CI, 0.713–0.801) OR: 1.68 (95%CI, 1.42-1.98)	NR
Moretti et al (2018)[35]	NUTRIC-CRP	High risk: 16.0	NR	Low risk: 9.5 $\pm$ 6.9 High risk: 14.8 $\pm$ 22.0	NR	NR
Auiwattanakul et al (2019)[41]	NRS-2002	Risk: 47.0	NR	NR	HR: 1.34 (95%CI, 0.98–1.85)	NR
Köseoğlu et al (2011)[24]	NRS-2002	High risk: 58.0	Correlation: 0.527*	NR	NR	NR
Küçükardali et al (2008)[25]	NRS-2002	Risk: 39.4	Low risk: 6.4 $\pm$ 5.5 High risk: 7.9 $\pm$ 6.3*	NR	NR	NR
Maciel et al (2019)[32]	NRS-2002	Risk: 51.9 High risk: 47.6	Low risk: 4.0 (2.0–10.0) High risk: 5.0 (3.0–8.0)	Low risk: 5.0 (1.0–10.0) High risk: 4.0 (2.0–8.0)	NR	NR

(continued)

Table 5 **Continued**

Reference	Tool	Nutritional risk prevalence (%)	Predictive validity			Nutrition intervention, risk score, and outcomes interaction
			ICU LOS	Duration of MV	28-day mortality	
Özbilgin et al (2016)[38]	NRS-2002	Risk: 80.3	Correlation: 0.118	Correlation: 0.161*	NR	NR
	MNA-SF	Risk: 61.8 Malnourished: 32.9	Correlation: −0.030	Correlation: −0.076	NR	NR
	mNUTRIC	High risk: 22.4	Correlation: −0.134	Correlation: 0.245*	NR	NR
Shpata et al (2015)[40]	NRS-2002	Risk: 62.6	OR ICU LOS > 14 days group aged ≥ 65 years: 1.80 (95%CI, 1.13–2.87)	NR	NR	NR
Chittawatanarat et al (2016)[45]	BNT/NT	Moderate risk: 9.3 High risk: 12.1	NR	NR	OR BNT/NT II: 2.06 (95%CI, 1.32–3.20) OR BNT/NT III: 4.04 (95%CI, 2.34–6.96) OR BNT/NT IV: 2.55 (95%CI, 1.43–4.53)	NR
Tripathy et al (2014)[42]	MUST	Medium and high risk: 47.7	NR	NR	Without risk: 17.1% Medium risk: 27.3% High risk: 42.3%*	NR
Ramírez et al (2008)[39]	NSR	Moderate risk: 30.7 High risk: 44.3	NR	NR	NR	NR

*Statistically significant ($P < 0.05$).

Abbreviations: aROC, area under the receiver operating characteristics curve; BNT/NT, Bhumibol Nutrition Triage/Nutrition Triage; CRP, C-reactive protein; HR, hazard ratio; ICU, intensive care unit; LOS, length of stay; MUST, Malnutrition Universal Screening Tool; MV, mechanical ventilation; MNA-SF, Mini Nutritional Assessment; mNUTRIC, modified Nutrition Risk in the Critically Ill score; NR, not reported; NUTRIC, Nutrition Risk in the Critically Ill; NRS-2002, Nutritional Risk Screening, NSR, Nutritional Score Risk; OR, odds ratio; RR, relative risk.

regression models were used in 8 studies[20,22,27,33,36,43,49,50,53] using mNUTRIC and predicted a high risk of death in patients with a high score in comparison with patients with a low score (range, 1.48[36] to 33.64[43]). On the other hand, 3 of 4 studies demonstrated a significant increase in death risk (range, 2.10[32] to 2.68[40]) in patients identified with NR by NRS-2002. A significant association between NR and death was also demonstrated in 1 study using Bhumibol Nutrition Triage/Nutrition Triage (BNT/NT)[45] and in another study using MUST as a screening tool.[42]

A significantly longer ICU LOS in patients with NR, when compared with patients without or with low NR, was demonstrated in 12[20,23,25,30,31,33,36,37,43,44,52,53] of 17 studies that performed this comparison by a bivariate analysis. Two studies reported a positive correlation between ICU LOS and NR when using NRS-2002; the correlation was 0.118 in 1 study[38] and 0.527 in the other.[24] On the other hand, Özbilgin et al[38] demonstrated a negative correlation of mNUTRIC (–0.134) and Mini Nutritional Assessment (MNA-SF; –0.030) with ICU LOS.[38] According to multivariate analysis, NR was a predictor of longer ICU LOS in all 3 studies that performed this analysis.[33,40,50] The risk for longer ICU LOS in patients with NR compared with patients without or with low NR ranged from 1.18[50] to 1.72[33] in studies using mNUTRIC and was 1.80[40] in the study using NRS-2002.

Nine studies compared the duration of MV between patients grouped according to NR by bivariate analysis, and a significantly longer duration of MV was found 5 of the 9 studies in patients with NR when compared with those without or with low NR.[30,36,37,44,50] Two studies reported the correlation between duration of MV and NR. It was equal to –0.076 in 1 study using the MNA-SF tool; the same study demonstrated a positive correlation with NRS-2002 (0.161) and mNUTRIC (0.245).[38] The second study also reported a positive correlation between NR and MV in patients (range, 0.162 with mNUTRIC to 0.195 with NUTRIC with C-reactive protein.[34] By multivariate analysis, NR was a predictor of longer MV duration in the 2 studies that performed this analysis, and the risk ranged from 1.46[33] to 1.54[50] in patients with NR compared with patients without or with low NR as assessed by mNUTRIC. One study evaluated the accuracy of mNUTRIC and MUST in predicting longer MV duration by aROC curve construction; the results were not clinically relevant.[48]

Interaction between caloric-protein balance and NR in outcome prediction

Among the included studies, 8 evaluated if a nutritional intervention could modify the association between NR score and clinical outcomes.[12,13,21,26,28,36,44,47] Six studies reported no significant difference in mortality rates in low-NR patients grouped according to the nutritional therapy,[12,13,21,28,36,44,47] whereas Lee et al[26] reported that the risk of death was 6.30 times higher in a group of patients at low NR who received at least two-thirds of their prescribed energy in comparison with those who received a lower amount of energy.[26] On the other hand, in patients at high NR, the results indicated the group that received adequate nutritional therapy (ie, energy and/or protein intake as defined by the authors) had a lower incidence of death compared with the control group.

The definition of adequate nutrition therapy was heterogeneous among studies and included parameters such as protein intake (a difference of 10% from the goal) and energy intake (a difference of 10% from the goal)[28,47]; reaching the amount of energy prescribed[12,13]; $\geq$ 25 kcal/kg for energy, and $\geq$ 1.2 g/kg for protein[21]; receiving at least two-thirds of prescribed energy[26]; every 1000 extra kcal/d[36]; and energy intake $\geq$ 800 kcal/d.[44]

DISCUSSION

In this systematic review, NR data of critically ill patients were evaluated by an analysis of 36 studies.[12,13,20–53] Eight screening nutritional tools were applied among the eligible studies and the prevalence of NR ranged from 16.0%[35] to 99.5%.[32] The most frequently used screening tools were mNUTRIC (in 26 studies[13,20–23,26–31,33,34,36–38,43,44,46–53]) and NRS-2002 (in 7 studies[24,25,32,38,40,41,53]). Nutritional risk was an independent predictor of 28-day mortality,[20,33,36,45,49] longer ICU LOS,[33,40,50] and duration of MV[33,50] in some of the studies evaluated. Data about interaction between caloric-protein balance and NR in the outcome prediction are heterogeneous.

To our knowledge, there is no systematic review of NR prevalence and its association with clinical outcomes in critically ill patients. The prevalence of NR was widely variable, which probably can be explained by the different tools applied in the studies and, mainly, the heterogeneous sample analyzed. Higher NR prevalence in clinical ICUs in comparison with surgical and mixed ICUs was observed, which probably was associated with the number and severity of comorbidities of patients admitted to clinical ICUs. In fact, in 1 of the studies with highest prevalence of NR (88.7%), the median of APACHE score was 22.0,[21] whereas in the study with lowest NR prevalence (16.0%), the mean APACHE score was 16.7.[35] A systematic review including 20 observational studies about the prevalence of malnutrition in critically ill patients also demonstrated a wide

variability in the prevalence of this condition (range, 5.0% to 82.0%), and NR prevalence was higher in patients with acute kidney injury compared with patients admitted for cardiac surgery. It is important to reinforce that in studies included in this review, the tools applied for malnutrition diagnosis included nutritional screening tools, such as NRS-2002.[54]

A recent systematic review summarized data of 12 studies using mNUTRIC score for assessment of NR[14]; however, the authors did not include 16 studies[20–22,28–31,37,43,44,46,49–53] that were eligible for the present review. Two studies[55,56] were included in the review performed by Reis et al[14] but they did not meet our inclusion criteria because the association between NR and outcomes were not assessed and because of the method adopted for NR screening. The authors concluded the mNUTRIC score is related to clinical outcomes such as LOS and is appropriate for use in critically ill patients. In fact, a narrative review about NR in critically ill patients[57] suggested the mNUTRIC should be used. The results of the present systematic review corroborate this recommendation if we consider that it was an independent predictor of death in all studies that performed a multivariate analysis. However, the evidence on the predictive validity of this tool, considering the duration of ICU and MV, is scarce; it has been evaluated in < 5 studies. Regarding the NRS-2002, the predictive validity demonstrated in some studies included in the present review is questionable because the limited number of studies in which a multivariate analysis was performed to assess this added to the different cutoff points adopted for the NR classification (≥ 3 points or ≥ 5 points).

The validity of mNUTRIC in predicting worse clinical outcomes is expected because it includes disease severity–related variables such as APACHE II and SOFA, which are recognized predictors of mortality and clinical outcomes.[58,59] Considering that these tools do not consider any classic and direct nutritional parameters,[57] their applicability as an indicator of NR is questionable because the prognostic performance is not the same as predicting the interaction between NR in support and nutritional outcomes.[29,60] In addition, indirect long-term and short-term variables resulting in reduced food intake as well as recent weigh loss evaluated by "number of comorbidities" and "days from hospital to ICU admission"[12] probably cannot be assessed by ≥ 2 comorbidities and only ≥ 1 day of hospital stay.

Regarding the ability to identify patients in the ICU who will benefit most from nutritional support, currently, to our knowledge, no screening tool has elucidated this effect. In this review, 7 of 8 studies that evaluated this interaction were from a single center and observational.[12,21,26,28,36,44] Thus, future multicenter prospective studies and randomized controlled trials enrolling patients at high versus low risk for NR in the ICU are necessary for additional confirmation.[12,13,21,26,28,47] Moreover, a systematic review of 7 randomized clinical trials demonstrated divergences between the concepts of "permissive" and "trophic" underfeeding, varying from 20.0% to 60.0% of energy requirements.[61] Thus, to establish nutritional intervention, risk score, and outcome interactions, it is essential to first standardize these key concepts.

Different nutritional screening tools validated in noncritically ill patients were applied in the studies included in this review. It is important to reinforce that a common feature among these tools (ie, NRS-2002, MNA, MUST, NSR, and BNT/NT) is that they are composed of historical nutrition variables and history of weight loss in the past 6 months. However, this information requires conscious patients or relatives with knowledge about these aspects to establish an NR score, which is not easy and common, or may be inaccurate in this scenario, considering our experience in ICUs. In particular, the NRS-2002 classifies a patient as at risk if the APACHE II score is > 10; thus, most patients in the ICU would be considered at risk regardless of nutritional parameters.[57,60] ASPEN proposed that an NRS-2002 score ≥ 5 points should be adopted as a cutoff for NR in ICUs.[6] In fact, when this cutoff was adopted in Brazilian studies, the authors showed a NR prevalence of 47.6% and 55%, and it was associated with worse clinical outcomes.[32,53] In the present review, only these 2 studies[32,53] adopted this cutoff for NR classification and no study was found that looked at the feasibility of applying the NRS-2002 in the ICU. According to the latest position of the Academy of Nutrition and Dietetics, the MST should be used to screen adults for malnutrition regardless of their age, medical history, or setting.[62] However, no 1 study included in the present review applied this screening tool to confirm this validity in ICU setting.

Risk of bias was identified in 69.7% of the included studies,[12,13,20,21,23–26,28–31,34,35,37–39,41,43,44,46,48,49] which makes the quality of evidence on NR in the ICU questionable. For observational studies, there is a lack of consensus on the best risk assessment tool; however, NOS is one of the best-known scales for assessing the quality and risk of bias in studies with these designs. Specific limitations are related to community representativeness, lack of definition of the "most important control factor" in the analyses and results, and lack of differentiation of studies that blind the results from those that evaluated the results through database records.[63] Another weakness of the NOS is lack of recommendation on how to evaluate and report the score.

In this systematic review, we used the cutoffs <7 and ≥ 7, proposed by Veronese et al.[19]

The present review was conducted following the Cochrane protocols[16] and using 3 large electronic databases. The strengths of this review include a preregistration protocol that did not limit the literature search to specific languages or periods. A meta-analysis was not performed because of the heterogeneity between studies, especially regarding the nutritional screening tools, outcomes measurements, and the few multivariate statistical models. The quality of the body of evidence using the Grading of Recommendations Assessment, Development and Evaluation approach[64] could not be evaluated because effect size and associated confidence intervals could not be assessed because no meta-analysis was performed.

The state of NR in critically ill patients could be reached by a combination of low or moderate degrees of impaired nutritional status and low or moderate degrees of disease severity (stress metabolism). It should be noted that the term "nutritional risk" in this context refers to the risk of acquiring complications and other forms of adverse outcomes that might have been prevented by timely and adequate nutrition support.[60] Considering this and the evidence presented in this systematic review, it is suggested that a tool for nutritional screening in the ICU include the following 3 concepts: (1) a severity disease score; (2) at least 1 nutritional parameter such as reduce food intake, recent weight loss, or physical examination; and (3) it should be simple and quick to use, with high sensitivity (its viability needs to be assessed). In fact, according to Preiser,[65] the inclusion of more nutrition-related indices in the model, such as the tolerance to enteral feeding, or the magnitude of the catabolic response (eg, insulin resistance, nitrogen balance) could enhance the specificity of a nutritional score. In addition, its predictive validity should be tested in robust studies that perform multivariate analysis to predict clinical outcomes. After this, a randomized controlled trial should be performed to establish whether NR is really a determinant in the interaction between nutritional supply and clinical outcomes.

CONCLUSION

The prevalence of NR in critically ill patients varies widely, which probably can be explained by the different tools applied and the heterogeneity of patients assessed. In fact, the identification of NR in critically ill patients is not a simple and straightforward practice, but it is clinically relevant. Despite their inherent limitations, NRS-2002 and mNUTRIC could be the current available tools for the evaluation of NR, because of their predictive validity demonstrated in available literature. However, additional research regarding the best tool for NR assessment in ICU and the interaction among it, nutritional supply, and clinical outcomes is necessary.

Acknowledgments

Author contributions. A.C. and F.M.S. conceptualized and designed the work and conducted the literature search. A.C., I.C.E., J.E.B., and F.M.S. assessed studies for eligibility and risk of bias and extracted data from included studies. A.C., I.C.E., R.F.T., and F.M.S. contributed to the interpretation of study data and drafted the manuscript. R.F.T. and J.E.B. revised the content of the final review. All authors approved the final version of the manuscript.

Funding. This work was supported by a Fundação de Amparo à Pesquisa do Estado do Rio Grande do Sul grant (F.M.S.); the funder had no role in the undertaking, data analyses, or reporting of this systematic review.

Declaration of interest. The authors have no relevant interests to declare.

Supporting Information

The following Supporting Information is available through the online version of this article at the publisher's website

Figure S1. **Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2009 checklist.**

REFERENCES

1. Robinson D, Walker R, Adams SC, et al. American Society for Parenteral and Nutrition (A.S.P.E.N.) definition of terms, enteral style, and conventions used in A.S.P.E.N. Board of Directors – approved documents. 2018. Available at: https://www.nutritioncare.org/uploadedFiles/Documents/Guidelines_and_Clinical_Resources/ASPEN Definition of Terms, Style, and Conventions Used in ASPEN Board of Directors–Approved Documents.pdf. Accessed November 20, 2019.
2. Kondrup J, Rasmussen HH, Hamberg O, et al. Nutritional risk screening (NRS 2002): a new method based on an analysis of controlled clinical trials. *Clin Nutr.* 2003;22:321–336.
3. Correia M. Nutrition screening vs nutrition assessment: what's the difference? *Nutr Clin Pract.* 2017;33:088453361771966–088453361771972.
4. Kondrup J, Allison SP, Elia M, et al. ESPEN guidelines for nutrition screening 2002. *Clin Nutr.* 2003;22:415–421.
5. Castro MG, Ribeiro PC, Souza IA de O, et al. Diretriz brasileira de terapia nutricional no paciente grave. *Braspen J.* 2018;33:2–36.
6. McClave SA, Taylor BE, Martindale RG, et al. Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) *JPEN J Parenter Enteral Nutr.* 2016;40:159–211.

7. Van Bokhorst-de van der Schueren MAE, Guaitoli PR, Jansma EP, et al. Nutrition screening tools: does one size fit all? A systematic review of screening tools for the hospital setting. *Clin Nutr*. 2014;33:39–58.
8. Rabito EI, Marcadenti A, da Silva Fink J, et al. Nutritional Risk Screening 2002, Short Nutritional Assessment Questionnaire, Malnutrition Screening Tool, and Malnutrition Universal Screening Tool are good predictors of nutrition risk in an emergency service. *Nutr Clin Pract*. 2017;32:526–532.
9. Garcia RS, Tavares L. R d C, Pastore CA. Rastreamento nutricional em pacientes cirúrgicos de um hospital universitário do sul do Brasil: o impacto do risco nutricional em desfechos clínicos the impact of nutritional risk in clinical outcomes. *Eistein*. 2013;11:147–152.
10. Gomes F, Emery PW, Weekes CE. Risk of malnutrition is an independent predictor of mortality, length of hospital stay, and hospitalization costs in stroke patients. *J Stroke Cerebrovasc Dis*. 2016;25:799–806.
11. Raslan M, Gonzalez MC, Gonçalves Dias MC, et al. Comparison of nutritional risk screening tools for predicting clinical outcomes in hospitalized patients. *Nutrition*. 2010;26:721–726.
12. Heyland DK, Dhaliwal R, Jiang X, et al. Identifying critically ill patients who benefit the most from nutrition therapy: the development and initial validation of a novel risk assessment tool. *Crit Care*. 2011;15:R268–11.
13. Rahman A, Hasan RM, Agarwala R, Martin C, et al. Identifying critically-ill patients who will benefit most from nutritional therapy: Further validation of the "modified NUTRIC" nutritional risk assessment tool. *Clin Nutr*. 2016;35:158–162.
14. Reis AM, Fructhenicht AVG, Moreira LF. Uso do escore NUTRIC pelo mundo: uma revisão sistemática. *Rev Bras Ter Intensiva*. 2019;31:379–385.
15. Singer P, Blaser AR, Berger MM, et al. ESPEN guideline on clinical nutrition in the intensive care unit. *Clin Nutr*. 2019;38:48–79.
16. Higgins JPT, Thomas J, Chandler J, et al. eds. *Cochrane Handbook for Systematic Reviews of Interventions, Version 6.0*, 2019. Available at: https://training.cochrane.org/handbook/current. Accessed November 20, 2019.
17. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *PLoS Med*. 2009;6:e1000100.
18. Wells G, Shea B, O'Connell D, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. Available at: http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp. Accessed November 20, 2019.
19. Veronese N, Cereda E, Solmi M, et al. Inverse relationship between body mass index and mortality in older nursing home residents: a meta-analysis of 19,538 elderly subjects. *Obes Rev*. 2015;16:1001–1015.
20. Jeong DH, Hong SB, Lim CM, et al. Comparison of accuracy of NUTRIC and modified NUTRIC scores in predicting 28-day mortality in patients with sepsis: a single center retrospective study. *Nutrients*. 2018;10: E 911.
21. Jeong DH, Hong S-B, Lim C-M, et al. Relationship between nutrition intake and 28-day mortality using modified NUTRIC score in patients with sepsis. *Nutrients*. 2019;11:e1906.
22. José IB, Leandro-Merhi VA, de Aquino JLB, et al. The diagnosis and NUTRIC score of critically ill patients in enteral nutrition are risk factors for the survival time in an intensive care unit? *Nutr Hosp*. 2019;36:1027–1036.
23. Kalaiselvan M, Renuka M, Arunkumar A. Use of Nutrition Risk in Critically ill (NUTRIC) score to assess nutritional risk in mechanically ventilated patients: a prospective observational study. *Indian J Crit Care Med*. 2017;21:253–256.
24. Koseoglu Z, Kuvvetli A, Kosenli O, et al. Increased nutritional risk in major trauma: correlation with complications and prolonged length of stay. *Ulus Travma Acil Cerrahi Derg*. 2011;17:521–524.
25. Küçükardali Y, Yazgan Y, Solmazgül E, et al. Malnutrition screening with the nutritional risk screening 2002 in internal medicine service and the intensive care unit. *Anatol J Clin Invest*. 2008;2:19–24.
26. Lee ZY, Noor Airini I, Barakatun-Nisak MY. Relationship of energy and protein adequacy with 60-day mortality in mechanically ventilated critically ill patients: a prospective observational study. *Clin Nutr*. 2018;37:1264–1270.
27. Lew CCH, Cheung KP, Chong MFF, et al. Combining 2 commonly adopted nutrition instruments in the critical care setting is superior to administering either one alone. *J Parenter Enter Nutr*. 2018;42:872–876.
28. Lew CCH, Wong GJY, Cheung KP, et al. When timing and dose of nutrition support were examined, the modified Nutrition Risk in Critically Ill (mNUTRIC) score did not differentiate high-risk patients who would derive the most benefit from nutrition support: a prospective cohort study. *Ann Intensive Care*. 2018;8:1–13.
29. Lew CCH, Wong GJY, Cheung KP, et al. The association between nutritional adequacy and 28-day mortality in the critically ill is not modified by their baseline nutritional status and disease severity. *Crit Care*. 2019;23:11.
30. Ata ur-Rehman HM, Ishtiaq W, Yousaf M, et al. Modified nutrition risk in critically ill (mNUTRIC) score to assess nutritional risk in mechanically ventilated patients: a prospective observational study from the Pakistani population. *Cureus*. 2018;10:e3786.
31. MacEachern KN, Kraguljac AP, Mehta S. Nutrition care of critically ill patients with leukemia: A retrospective study. *Can J Diet Pract Res*. 2019;80:34–38.
32. Maciel L. R M d A, Franzosi OS, Nunes DSL, et al. Nutritional risk screening 2002 cut-off to identify high-risk is a good predictor of ICU mortality in critically ill patients. *Nutr Clin Pract*. 2019;34:137–141.
33. Mendes R, Policarpo S, Fortuna P, et al. Nutritional risk assessment and cultural validation of the modified NUTRIC score in critically ill patients - a multicenter prospective cohort study. *J Crit Care*. 2017;37:45–49.
34. Moretti D, Bagilet DH, Buncuga M, et al. Estudio de dos variantes de la puntuacion de riesgo nutricional "NUTRIC" en pacientes criticos ventilados. *Nutr Hosp*. 2014;29:166–172.
35. Moretti D, Ré MD, Rocchetti NS, et al. Relationship between the NUTRIC nutritional risk scale and protein hypercatabolism in critically ventilated patients. *Nutr Hosp*. 2018;35:1263–1269.
36. Mukhopadhyay A, Henry J, Ong V, et al. Association of modified NUTRIC score with 28-day mortality in critically ill patients. *Clin Nutr*. 2017;36:1143–1148.
37. Mukhopadhyay A, Tai BC, Remani D, et al. Nutritional risk assessment at admission can predict subsequent muscle loss in critically ill patients. *Eur J Clin Nutr*. 2018;72:1187–1190.
38. Özbilgin Ş, Hanci V, Ömür D, et al. Morbidity and mortality predictivity of nutritional assessment tools in the postoperative care unit. *Medicine (Baltimore)*. 2016;95:1–7.
39. Ramírez A, Rendon C, Valencia E. Puntaje de detección de riesgo nutricional en pacientes criticamente enfermos (NSRR: Nutritional Score Risk Research). *Nutr Hosp*. 2008;23:505–512.
40. Shpata V, Ohri I, Nurka T, et al. The prevalence and consequences of malnutrition risk in elderly Albanian intensive care unit patients. *Clin Interv Aging*. 2015;10:481–486.
41. Auiwattanakul S, Chittawatanarat K, Chaiwat O, et al. Effects of nutrition factors on mortality and sepsis occurrence in a multicenter university-based surgical intensive care unit in Thailand (THAI-SICU study). *Nutrition*. 2019;58:94–99.
42. Tripathy S, Mishra JC, Dash SC. Critically ill elderly patients in a developing world–mortality and functional outcome at 1 year: a prospective single-center study. *J Crit Care*. 2014;29:474.e7–474.e13.
43. Tsai M-H, Huang H-C, Peng Y-S, et al. Nutrition risk assessment using the modified NUTRIC score in cirrhotic patients with acute gastroesophageal variceal bleeding: prevalence of high nutrition risk and its independent prognostic value. *Nutrients*. 2019;11:2152.
44. Wang CY, Fu PK, Te Huang C, et al. Targeted energy intake is the important determinant of clinical outcomes in medical critically ill patients with high nutrition risk. *Nutrients*. 2018;10:e1731.
45. Chittawatanarat K, Chaiwat O, Morakul S, et al. Outcomes of nutrition status assessment by bhumibol nutrition triage/nutrition triage (BNT/NT) in multicenter THAI-SICU study. *J Med Assoc Thai*. 2016;99:S184–S192.
46. Chourdakis M, Grammatikopoulou MG, Poulia KA, et al. Translation of the modified NUTRIC score and adaptation to the Greek ICU setting. *Clin Nutr ESPEN*. 2019;29:72–76.
47. Compher C, Chittams J, Sammarco T, et al. Greater protein and energy intake may be associated with improved mortality in higher risk critically ill patients: a multicenter, multinational observational study. *Crit Care Med*. 2017;45:156–163.
48. de Vries MC, Koekkoek W, Opdam MH, et al. Nutritional assessment of critically ill patients: validation of the modified NUTRIC score. *Eur J Clin Nutr*. 2018;72:428–435.
49. Gonzalez MC, Bielemann RM, Kruschardt PP, et al. Complementarity of NUTRIC score and Subjective Global Assessment for predicting 28-day mortality in critically ill patients. *Clin Nutr*. 2019;38:2846–2850.
50. Hsu PH, Lee CH, Kuo LK, et al. Higher energy and protein intake from enteral nutrition may reduce hospital mortality in mechanically ventilated critically ill elderly patients. *Int J Gerontol*. 2018;12:285–289.
51. Brascher JMM, Peres WAF, Padilha PC. Use of the modified "Nutrition Risk in the critically ill" score and its association with the death of critically ill patients. *Clin Nutr ESPEN*. 2020;35:162–166. https://doi.org/10.1016/j.clnesp.2019.10.005
52. Càndido ACO, SCPDutra L. Nutritional risk in critical patients using the Nutric Score Risk method. *Nutr Clín Diet Hosp*. 2019;39:19–25.
53. Marchetti J, Reis AM, Santos AF, et al. O elevado risco nutricional está associado a desfechos desfavoráveis em pacientes internados na unidade de terapia intensiva. *Rev Bras. Ter Intensiva*. 2019;31:326–332.
54. Lew CCH, Yandell R, Fraser RJL, et al. Association between malnutrition and clinical outcomes in the intensive care unit: a systematic review. *JPEN J Parenter Enteral Nutr*. 2017;41:744–758.
55. Rosa M, Heyland DK, Fernandes D, et al. Translation and adaptation of the NUTRIC score to identify critically ill patients who benefit the most from nutrition therapy. *Clin Nutr ESPEN*. 2016;14:31–36.
56. Coltman A, Peterson S, Roehl K, et al. Use of 3 tools to assess nutrition risk in the intensive care unit. *JPEN J Parenter Enteral Nutr*. 2015;39:28–33.
57. Lee ZY, Heyland DK. Determination of nutrition risk and status in critically ill patients: what are our considerations?. *Nutr Clin Pract*. 2019;34:96–111.
58. Knaus W, Draper E, Wagner D, et al. APACHE II: a severity of disease classification system. *Crit Care Med*. 1985;13:818–829.

59. Vincent JL, Moreno R, Takala J, et al. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. *Intensive Care Med*. 1996;22:707–710.
60. Kondrup J. Nutritional-risk scoring systems in the intensive care unit. *Curr Opin Clin Nutr Metab Care*. 2014;17:177–182.
61. Silva CFA, de Vasconcelos SG, da Silva TA, et al. Permissive or trophic enteral nutrition and full enteral nutrition had similar effects on clinical outcomes in intensive care: a systematic review of randomized clinical trials. *Nutr Clin Pract*. 2018;33:388–396.
62. Skipper A, Coltman A, Tomesko J, et al. Position of the academy of nutrition and dietetics: malnutrition (undernutrition) screening tools for all adults. *J Acad Nutr Diet* 2019;piiS2212-2672:31366–31368.
63. Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. *Eur J Epidemiol*. 2010;25:603–605.
64. Balshem H, Helfand M, Schünemann HJ, et al. GRADE guidelines: 3. Rating the quality of evidence. *J Clin Epidemiol*. 2011;64:401–406.
65. Preiser J-C. Do we need an assessment of the nutrition risk in the critically ill patient? *Crit Care*. 2012;16:101–102.