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Nutritional risk assessment and cultural validation of the modified NUTRIC score in critically ill patients—A multicenter prospective cohort study

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ABSTRACT

Purpose: Characterize the nutritional risk of critically ill patients with the modified NUTrition Risk in the Critically ill (NUTRIC) score.
Materials: National, multicenter, prospective, observational study conducted in 15 polyvalent Portuguese intensive care unit (ICU), during 6 months. Adult patients were eligible. Those transferred from another ICU or readmitted, brain dead at admission, and with length of ICU stay (LOS) of 72 hours or less were excluded. NUTRIC score was calculated at admission; scores ≥5 represent a high nutritional risk. Main outcome was mortality from all causes at 28 days after admission to the ICU; LOS and days without mechanical ventilation (days free of MV) were secondary outcomes.
Results: From 2061 admissions, 1143 patients were considered, mostly males (n = 744, 64.7%) with median (P_{25}-P_{75}) age of 64 (51-75). Patients at high nutritional risk were 555 (48.6%). High NUTRIC score was associated with longer LOS ($P < .001$), less days free of MV ($P = .002$) and higher 28-day mortality ($P < .001$). The area under the curve of NUTRIC score ≥5 for predicting 28-day mortality was 0.658 (95% CI, 0.620-0.696). NUTRIC score ≥5 had a positive predictive value 32.7% and a negative predictive value 88.8% for 28-day mortality.
Conclusions: Almost half of the patients in Portuguese ICUs are at high nutritional risk. NUTRIC score was strongly associated with main clinical outcomes.

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1. Introduction

Malnutrition is common in hospitalized patients and highly prevalent in the population of critically ill patients all around the world [1,2]. It is associated with increased morbidity, mortality and occurrence of nosocomial infections, prolonged hospitalization, worse functional status at discharge from the Intensive Care Units (ICU) and increased hospital costs [3,4].

In Portugal, data regarding the impact of malnutrition at hospital admission has demonstrated that the frequency of patients at nutritional risk is very high, comprising 29% to 47%, depending on the methodology used [5]. Data on Portuguese critically ill patients is still, to date, not available.

Most of the scores and tools to assess nutritional risk were validated in the hospital setting [6-12], and include a variety of criteria to identify nutritional risk, such as food/nutritional intake, physical examination, severity of illness, anthropometric data and functional assessment. Many of these criteria are difficult to obtain in critically ill patients since almost all of these patients require mechanical ventilation and sedation. Changes in weight can be influenced by fluid status, given the large volumes necessary to maintain hemodynamic stability, and consequently muscle and fat wasting evaluation become more difficult. Many traditional tools do not provide information regarding inflammatory status which is crucial in an ICU population, since it's one of the factors responsible for hypermetabolic status and hence, muscle wasting [13].

Based on the assumption that the nutritional risk is not the same for all critically ill patients, Heyland et al developed and validated the NUTrition Risk in the Critically ill (NUTRIC score), the first nutritional risk assessment tool developed specifically for the ICU population that could identify patients that require more aggressive nutritional support, based on their nutritional risk [14,15]. The conceptual model links patient predictor markers of acute and chronic starvation, acute and chronic inflammation and outcome. The severity of illness is derived from the use of the variables with traditional scores of severity of illness,

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the Acute Physiology and Chronic Health Evaluation II (APACHE II) score [16] and baseline Sequential Organ Failure Assessment (SOFA) [17].

The variables in the NUTRIC score are easy to obtain in the critical care setting, except Interleukin-6 (IL-6) level, which is not commonly measured. As it has already been demonstrated, the performance of the NUTRIC score varies only slightly when excluding IL-6 levels from the score or when this is replaced by another available inflammatory biomarker. The modified NUTRIC score (without IL-6) has been recently validated [18].

2. Objective

To characterize the nutritional risk of hospitalized patients in Portuguese ICU using the modified NUTRIC score.

3. Materials

A prospective, observational, multicentric cohort study was conducted in a convenient sample of tertiary polyvalent ICUs across Portugal. Nationwide, around 4100 patients per year were expected to be admitted in the ICUs. Polyvalent ICUs from public academic hospitals were considered eligible to participate. From the 30 identified ICUs, 23 expressed the will to participate and 15 ICUs provided the complete dataset for effective enrolment. All enrolled ICUs had allocated nutritional staff. Patients consecutively admitted to the participant ICUs were enrolled during a period of 6 months, in 2014, with only admission to the ICU being considered. Patients aged over 18 years were considered eligible for recruitment. Patients were excluded if diagnosed as being brain dead at admission or if they had been transferred from another ICU or readmitted into the ICU. Only patients with a length of ICU stay (LOS) of more than 72 hours were considered for analysis.

The transcultural adaptation of the tool was previously done as an independent part of the project. The process of cross-cultural adaptation followed the multistep approach, according to the international guidelines [19]. The original English version of the NUTRIC score was independently translated to Portuguese by two bilingual translators with specific skills in English and Portuguese and proved experience in the health sciences. A panel of experts (physicians, nurses and dietitians working in ICU) evaluated the two translations of NUTRIC score, by analyzing the phrasing of each item, and consensually obtaining the proposed version. An official translator, registered in the Portuguese Translators Society, proceeded to back-translate the proposed version to English, the language of the original version. The back-translated version was reviewed by the developers of the original tool to assess the adequateness of the content (content validity). A pilot study was conducted with 46 critically ill patients admitted in one of the ICU's from the study, to assess the understanding and applicability of the translated version of the modified NUTRIC Score. The cultural validation from English to Portuguese language has succeeded in achieving idiomatic, semantic, and conceptual equivalence between the original toll and the Portuguese version. The official endorsement of the proposed Portuguese version of the NUTRIC score was obtained.

The NUTRIC score, without IL-6 levels includes five variables: age, APACHE II, SOFA, number of co-morbidities and days from hospital to ICU admission. The score was calculated with data from the first 24 h after ICU admission. The NUTRC score ranges from zero to nine; a score ≥5 indicates a high nutritional risk [14]. Main outcome was mortality from all causes at 28 days after admission to the ICU; LOS and days without invasive mechanical ventilation (days free of MV) were secondary outcomes. Outcomes were collected until day 28, starting at admission to the ICU. Data were recorded from the patient chart (electronic and/or paper) following the standardized data collection procedures stated in the manual of procedures developed specifically for the study. Local researchers received training to collect data. The study was approved by the Ethics Committees for Health for every participant Hospitals and was licensed in the Portuguese Data Protection Authority (no. 6635/2013). As mandated by the same Authority, informed consent was obtained from all patients included.

Prevalence rates are presented with 95% confidence intervals (95% CI). Proportions are compared with binomial test, χ^2 test or Fisher exact test (as adequate). The normality of the distribution of the NUTRIC score was excluded. The association of the NUTRIC score with the three main outcomes (LOS, days off MV and 28-day mortality) was analyzed with Mann-Whitney *U* test and Spearman correlation, adjusted to confounding factors when needed. Logistic regression analysis was used to further characterize the association between the NUTRIC score and the three main outcomes, using odds ratio (OR) with 95% CI of the estimates; linear regression was performed but discarded due to rejection of the normality of the residuals. The model discrimination for predicting 28-day mortality was assessed by the area under the receiving operating characteristic curve (AUC) (interpretation: excellent ≥0.90, adequate 0.70-0.89, poor <0.70) and the generalized max-rescaled R-squared statistic.

The following software packages were used for analysis: OpenEpi (Dean AG, Sullivan KM, Soe MM. OpenEpi: Open Source Epidemiologic Statistics for Public Health. www.OpenEpi.com, Version 2015/05/04, accessed 2015/07/25), SISA (Uitenbroek, Daan G. SISA. 1997. http://www.quantitativeskills.com/sisa.htm. (2015/07/25)), SPSS 22.0 (SPSS for Windows, Rel. 22.0.1. 2013. SPSS Inc, Chicago, IL; EUA), Stata (StataCorp. 2013. Stata Statistical Software: Release 13. College Station, TX; StataCorp LP, USA) and VassarStats (Lowry R. VassarStats. http://vassarstats.net/. Vassar College, Poughkeepsie, NY, USA, accessed 2015/07/25).

4. Results

During the 6-month recruitment period, 2061 patients were eligible for enrolment in the 15 participating ICUs and 1143 were included in the analysis. Exclusion occurred in case the patient presented one of the previously established criteria: 26 were diagnosed brain dead at admission and 50 had been transferred from another ICU, informed consent was not obtained from 149 patients and LOS in the ICU was less than 72 hours in 670 patients; 23 patients were excluded from analysis due to incomplete data collection for obtaining the NUTRIC score.

Patients that were excluded had similar age distribution than the recruited sample, but a significantly lower proportion were males (58.2% vs 64.8%; $P = .002$) and had a significantly lower baseline APACHE II (median 17 vs 20; $P = .009$) and SOFA (median 5 vs 7; $P < .001$).

In the recruited sample, the median (P_{25}-P_{75}) age at admission was 64 (51-75) years. Males predominated (n = 740, 64.8%; $P < .001$). The median (P_{25}-P_{75}) baseline APACHE II and SOFA were 20 (14-26) and 7 (5-10), respectively. Primary admission diagnoses were respiratory (n = 262, 23.0%), sepsis (n = 230, 20.2%) and trauma (n = 167, 14.6%); 2 or more co-morbidities were present in 393 (34.4%) patients. Patients' baseline characteristics are summarized in Table 1.

The median (P_{25}-P_{75}) of the days free of MV was 2 (1-4) days and LOS was 9 (5-15) days. At day 28, 243 of 1122 patients with known status were deceased (21.7%; 95% CI, 19.35-24.16).

The median (P_{25}-P_{75}) of the NUTRIC score was 4 (3-6). There were 555 patients (48.6%; 95% CI, 45.67-51.45) at high nutritional risk (NUTRIC score ≥5). Patients at high nutritional risk had higher median (P_{25}-P_{75}) LOS 10 (5-16.5) days vs 8 (5-14) days ($P < .001$), less median (P_{25}-P_{75}) days free of MV 2 (1-4) days vs 3 (1-4) days ($P < .001$), and higher 28-day mortality 32.7% vs 11.2% ($P < .001$).

On logistic regression analysis, NUTRIC score ≥5 was associated with longer LOS (≥9 days) (OR 1.72; 95% CI, 1.36-2.17; $P < .001$; n = 1126), less days free of MV (≤2 days) (OR 1.46; 95% CI, 1.16-1.85; $P = .002$; n = 1124) and higher 28-day mortality (OR 3.84; 95% CI, 2.80-5.26; $P < .001$; n = 1122). A NUTRIC score ≥5 predicted 28-day mortality with AUC 0.658 (95% CI, 0.620-0.696) (Supplementary Fig. S1), with a positive predictive value of 32.7% (95% CI, 28.91-36.77) and a negative

predictive value of 88.8% (95% CI, 85.92-91.08) for 28-day mortality; its sensitivity was 73.25% (95% CI, 67.36-78.42) and specificity 58.4% (95% CI, 55.07-61.58). The 28-day mortality prediction of the NUTRIC score, at its full range, calculated by a logistic regression model, is compared with the observed mortality rate in Fig. 1. The NUTRIC score as a full scale (0-9) predicted 28-day mortality with AUC 0.718 (95% CI, 0.685-0.752) (Fig. 2 and Table 2).

The comparison between the sample characteristics and the results obtained in this study with those of the original validation study are presented in Table 2.

5. Discussion

Most of the critically ill patients admitted to the ICU show malnutrition criteria [20]. Critical illness is typically associated with a catabolic stress state, skeletal muscle weakness, and as consequence with complications such as increased infectious morbidity, multiple-organ dysfunction, difficult weaning, prolonged hospitalization, and increased mortality. The nutrition therapy is thought to help to attenuate the metabolic response to stress, prevent oxidative cellular injury and modulate immune responses. Delivering early nutrition support, by the enteral route if possible, is a strategy that reduces disease severity, complications, decreases LOS in the ICU and improves patient outcomes [13]. It is known that a poor nutritional status is associated with a worse outcome, but the reverse may not be true since there are other factors associated with illness or with the status of the patient that can negatively influence the outcome regardless of nutritional status.

The NUTRIC score, firstly validated by Heyland et al, is the first nutritional risk assessment tool developed specifically for the ICU population that can identify patients at risk for malnutrition. Later Rahman et al validated the modified NUTRIC, which allows the exclusion of the IL-6 levels, if not available, to assess nutritional risk at admission.

This study was the first to characterize the nutritional risk of hospitalized patients in Portuguese polyvalent ICUs; the study considered a large sample that was representative of annual ICU admissions in Portugal and it assessed prospectively the effectiveness of the modified NUTRIC score. High nutritional risk was present in half of the sample. As described in the original study [14,18] in our work NUTRIC score was associated with the target clinical outcomes; it had low positive predictive value (32.7%) and high negative predictive value (88.8%) to predict 28-day mortality. In this study patients at high nutritional risk had higher LOS, fewer days free of MV and increased 28-day mortality. The mean NUTRIC score in our study (4.4) is slightly (but not significantly) lower than that of the original validation of the NUTRIC score (4.7) [14] though clearly lower than that of the second validation of the score (5.5) [18]. The participants in this Portuguese (national) sample show significant differences on the variables included in the NUTRIC score when compared to the original validation group [14]. In the present study, participants were significantly older, had higher proportions of lower APACHE II scores, higher SOFA scores and a significantly lower proportion of participants had two or more co-morbidities. These differences are due to both the clinical variability of the patients treated in the ICU and the large size of the recruited sample in the present study. Despite these differences, this study finds the same association already described between NUTRIC score and main clinical outcomes, which endorses the use of toll in clinical settings with different demographic characteristics from the original validation group.

It was more frequent for patients to be admitted to hospital for more than 1 day before ICU admission in this study, compared to the original validation study which could possibly be interpreted as a marker of compromised nutritional intake and worse nutritional status. The 28-day mortality in this Portuguese national sample (21.7%) is similar to that of the original validation of the NUTRIC score (23.1%) [14] but it is lower than that observed in the second validation of the score (29%) [18]. The AUC is significantly higher in the original validation study but in both studies it is classified as "adequate". In spite of the clinical and statistical differences found between this study and other studies [14,18], the described performance of the NUTRIC score to predict 28-day mortality is clinically similar across these studies and the values of the AUC fit into the category of "adequate". However, this study was not planned to reassess the validation of the instrument, rather to use it to characterize a sample of patients from a national sample of polyvalent ICUs.

The main strengths of this study are the large size of this national sample, the prospective evaluation of the patients using a standardized protocol and the clinical heterogeneity provided by the number of participant ICUs. The unblinded nature of the study may have affected the clinicians' intervention, but in the absence of a uniformized therapeutic protocol and with such a large number of patients, admitted to many ICUs all over the country, any influence of biased interventions is probably minimized. The absence of data of nutritional support (either

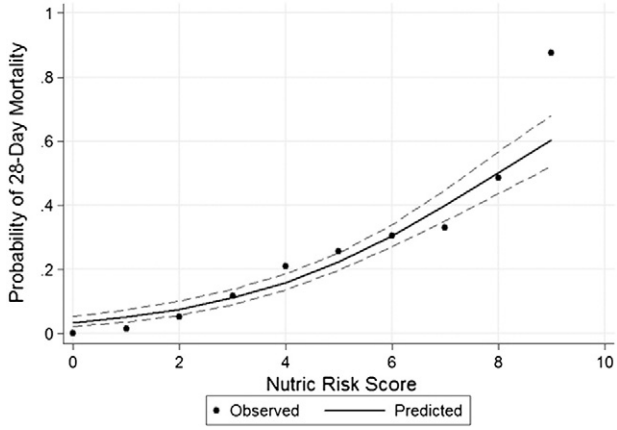

Fig. 1. The ability of the NUTRIC score to predict 28-day mortality. The graphic presents both the mortality rates which were observed (circles) and predicted by the logistic model (full line), the later with its 95% confidence interval (broken line).

Table 1
Clinical characteristics of the sample of recruited patients. Values are median (P_{25}-P_{75}) or n (%).

	Patients (n = 1143)
Age (years)	64 (51-75)
Gender	
Female	402 (35.2)
Male	740 (64.8)
Baseline APACHE II score	20 (14-26)
Baseline SOFA score	7 (5-10)
Days in hospital before ICU admission	1 (0-3)
BMI	26.2 (23.4-29.7)
Comorbidity	
Diabetes	184 (16.1)
Heart failure	143 (12.4)
Chronic pulmonary disease	138 (12.1)
Neoplasms	152 (13.3)
Chronic kidney disease	69 (6.0)
Brain stroke or transient ischemic event	64 (5.6)
Depression, anxiety or panic disorders	55 (4.8)
Hypertension	47 (4.1)
Chronic liver disease	48 (4.2)
Number of co-morbidities	1 (0-2)
Primary admission diagnosis	
Respiratory	262 (23.0)
Sepsis	230 (20.2)
Trauma	167 (14.6)
Post-operative conditions	159 (13.9)
Cardiovascular/vascular	118 (10.3)
Neurologic	108 (9.5)
Gastrointestinal	49 (4.3)
Metabolic	36 (3.2)
Renal	12 (1.1)

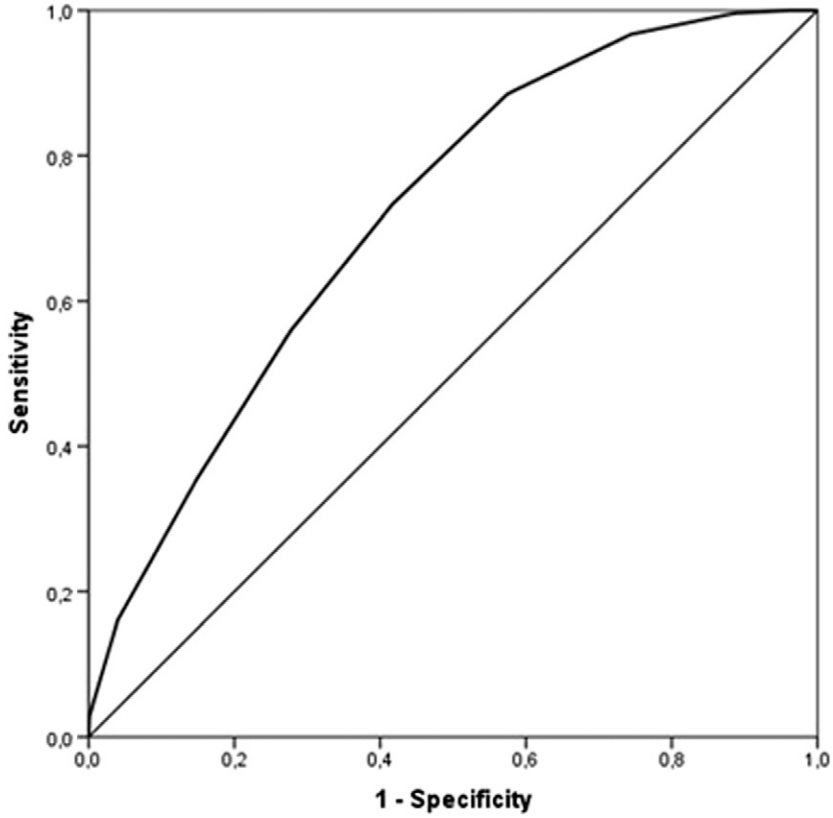

Fig. 2. Performance of the NUTRIC score as a full scale (0-9) to predict 28-day mortality in patients admitted to polyvalent intensive care units for at least 72 hours. AUC = 0.718 (95% CI, 0.685-0.752; n = 1122).

enteral or parenteral) during ICU stay, the convenience sample and the potential heterogeneity of therapeutic approaches are other weaknesses. The use of this tool on a daily basis for critically ill patients seems to have the advantage of raising the importance of nutritional support, drawing attention to high-risk patients for malnutrition. Considering that patients with high nutritional risk are expected to have more difficulty in achieving their nutritional needs, especially protein needs, we believe protocols should be implemented to optimize delivery of nutritional therapy such as earlier introduction of motility agents higher threshold of tolerance to gastric residual volume, and a volume based strategy for delivery of enteral feeding (as opposed to an hourly based strategy). If the strategies mentioned fail to achieve the nutritional needs, those patients should be selected for supplementary parenteral nutritional. More prospective studies investigating witch nutritional interventions could positively modify the patients prognosis based on the NUTRIC score should be done in the near future.

Table 2
Values of the NUTRIC score system in the original development sample, the second validation study and in this effectiveness study sample. Comparisons refer to the original study vs the present effectiveness study.

Variables in NUTRIC score	NUTRIC scoring system		Original development sample (14) (n = 598)	Second validation sample (18) (n = 1199)	Effectiveness study Sample (n = 1143)	*P*
	Range	Points				
Age	<50	0	130 (21.7)	199 (16.6)	255 (22.3)	
	50-75	1	345 (57.7)	710 (59.2)	574 (50.2)	.003
	≥75	2	123 (20.6)	290 (24.2)	314 (27.5)	
APACHE II	<15	0	111 (18.6)	48 (4.0)	292 (25.6)	
	15 - <20	1	135 (22.6)	157 (13.1)	257 (22.5)	
	20 - <28	2	226 (37.8)	508 (42.4)	374 (32.7)	.007
	≥28	3	126 (21.1)	486 (40.5)	219 (19.2)	
SOFA	<6	0	220 (36.8)	157 (13.1)	376 (32.9)	
	6 - <10	1	247 (41.3)	624 (52.0)	436 (38.1)	.007
	≥10	2	131 (21.9)	418 (34.9)	331 (29.0)	
Co-morbidities	0-1	0	160 (26.8)	392 (32.7)	750 (65.6)	
	≥2	1	438 (73.2)	807 (67.3)	393 (34.4)	<.001
Days from hospital to ICU admission	<1	0	375 (62.7)	757 (63.1)	466 (40.6)	
	≥1	1	223 (37.3)	442 (36.9)	678 (59.4)	<.001
IL6	<400	0	489 (81.8)	-	-	
	≥400	1	109 (18.2)	-	-	
Score range (IQR)			0-10 (3-6)	0-9 (4-7)	0-9 (3-6)	
Score mean (SD)			4.7 (2.2)	5.5 (1.6)	4.4 (2.1)	.086
AUC			0.783	0.783	0.718	.232
Gen R-Squared			0.169	0.169	0.103	
Gen Max-rescaled R-Squared			0.256	0.256	0.158	

6. Conclusion

The modified NUTRIC score, the first nutritional risk assessment tool developed and validated specifically for critically ill patients, demonstrated that in ICU Portuguese patients, despite presenting different characteristics from the original validated sample, a good correlation with main clinical outcomes.

The modified NUTRIC score can be used widely and systematically, contributing to discriminate ICU patients at high nutritional risk. The cross-cultural adaptation of NUTRIC score demonstrated translation reliability and is acceptable to be used in critically ill patients.

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.jcrc.2016.08.001.

Statement of authorship

All authors were responsible for the study design, writing and revising of the manuscript. MA and DA were also responsible for the statistical analysis and data interpretation.

Conflict of interest statement

None declared.

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