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Modified Nutrition Risk in the Critically ill (mNUTRIC Score) as prognostic marker in critically ill cancer patients

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RESUMO

Objetivo: Relacionar o NUTRIC score modificado com os desfechos clínicos de pacientes oncológicos críticos. **Métodos:** Estudo prospectivo observacional, onde os pacientes foram acompanhados por 28 dias após a admissão na Unidade de Terapia Intensiva (UTI). Os dados foram coletados em prontuário físico e/ou eletrônico e o *mNUTRIC score* foi realizado em até 48 horas da admissão na UTI. A correlação de *Spearman* e a regressão logística univariada e multivariada foram utilizadas correlacionando os desfechos clínicos de interesse. **Resultados:** Trinta e cinco pacientes foram incluídos no estudo. Destes, 62,9% apresentavam alto risco nutricional. Pacientes que obtiveram pontuação mais alta no *mNUTRIC score* tinham idade mais avançada, pior *Performance Status*, Proteína C-Reativa maior, maior necessidade de instalação de VM e internação na UTI mais prolongada. Houve correlação forte entre o *mNUTRIC score* e utilização de ventilação mecânica (VM). O modelo de regressão logística multivariada demonstrou que pacientes com alto risco nutricional apresentavam 97,54 vezes mais chance de utilização de VM do que aqueles com baixo risco nutricional. **Conclusão:** O *mNUTRIC score* foi efetivo como preditor de utilização de VM e maior tempo de internação na UTI. Este instrumento demonstrou viabilidade para utilização e identificação inicial dos pacientes oncológicos críticos que necessitam de intervenção nutricional precoce.

Palavras-chave: Cuidados Críticos; neoplasias; avaliação nutricional.

ABSTRACT

Purpose: To relate modified nutritional risk in the critically ill (mNUTRIC score) with the clinical outcomes of critically ill cancer patients. **Methods:** A prospective observational study, in which they were followed up for 28 days after admission to the Intensive Care Unit (ICU). Data were collected in physical and/or electronic medical records and the mNUTRIC score was performed within 48 hours of admission to the ICU. Spearman's correlation and univariate and multivariate logistic regression were applied by correlating the clinical outcomes of interest. **Results:** Thirty-five patients were included in the study. Of these, 62.9% presented high nutritional risk. Patients who scored higher on the mNUTRIC score were older, worse Performance Status, higher C-Reactive Protein, greater need for MV installation and longer ICU stay. There was a strong correlation between the mNUTRIC score and the use of mechanical ventilation (MV). The multivariate logistic regression model showed that patients with nutritional risk were 97.54 times more likely to use MV. **Conclusion:** The mNUTRIC score was effective as a predictor of MV use and longer ICU stay. This instrument demonstrated viability for the initial use and identification of these patients who require early nutritional intervention.

Key-words: Critical care; neoplasms; nutrition assessment

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1. INTRODUCTION

According to estimates by the National Cancer Institute (INCA) for Brazil, in the biennium of 2018-2019 will occur about 420 thousand new cases of cancer, with the exception of non-melanoma skin cancer (INCA, 2017).

Individuals with malignant diseases have been increasingly admitted to Intensive Care Units (ICUs). A recent study indicates that about 18% of ICU beds are occupied by cancer patients (SOARES et al., 2016).

The relationship between malnutrition and cancer is well established in the literature, since it is the most common secondary diagnosis in cancer patients (THORESEN et al., 2013). The nutritional status deficit and the depletion of lean mass presented by the critically ill cancer patient are closely related to a decrease in the response to chemotherapy, radiotherapy or surgery, quality of life and functional capacity, increasing the risk of infections, post-operative time, hospitalization time and death occurrence (KYLE; PICCOLI; PICHARD, 2003). Thus, malnutrition must be detected and prevented as early as possible (BARBOSA-SILVA, 2008; POZIOMYCK et al., 2012).

However, nutritional assessment in critically ill patients is a challenge, since the traditional tools to assess the degree of malnutrition in these patients are limited (SINGER; DOIG; PICHARD, 2014) due to metabolic and hydration alterations, difficulty in mobilizing these patients, bed restriction and need for mechanical ventilation (MV) or sedation that may prevent the collection of previous data prior to hospitalization due to the level of consciousness (CRUZ et al., 2006). Thus, the need for a tool to assess the specific nutritional risk for this population was evident.

Heyland et al. (2011) developed a specific score for critically ill patients with the objective of quantifying the risk of adverse effects that could be modified through Nutrition Risk in the Critical ill (NUTRIC score). The NUTRIC score takes into account parameters such as Sepsis-related Organ Failure Assessment I (SOFA I), Acute Physiology and Chronic Health Evaluation II (APACHE II), age, number of comorbidities,

days of hospitalization prior to ICU admission, and Interleukin 6 (IL-6).

However, the dosage of IL-6 has not been easily applied in clinical practice. Thus, the modified NUTRIC score (mNUTRIC score) was proposed, which is an adaptation of the NUTRIC score, except for the IL-6 score in the score (RAHMAN et al., 2016). According to this tool, patients classified as high nutritional risk score (mNUTRIC Score ≥ 5) are more prone to worse clinical outcomes such as MV use and mortality (MENDES et al., 2017). The mNUTRIC score was validated by Rahman et al. (2016) and translated into Portuguese by Mendes et al. (2017).

Currently, many studies (CHOURDAKIS et al., 2018; JEONG et al., 2018; LEE; NOOR AIRINI; BARAKATUN-NISAK, 2018; MORETTI D, RÉ MD, ROCCHETTI NS, BAGILET DH, SETTECASE CJ, 2018) have been conducted using mNUTRIC score as a tool for nutritional assessment and screening in critically ill patients, however its applicability in cancer patients needs to be studied. Thus, the objective of this study was to relate the mNUTRIC score to the clinical outcomes of critically ill cancer patients.

2. MATERIALS AND METHODS

2.1. Study population

A prospective, observational study in which the relationship of a nutritional screening instrument (mNUTRIC score) with clinical variables and prognostic and severity factors of cancer patients admitted to the ICU was evaluated.

It was carried out between April and November 2018 and included individuals of both sexes, aged 20 years or older, diagnosed with malignant neoplasm and systemic inflammatory response syndrome (SIRS) or sepsis, and who were admitted to the ICU of Cancer Hospital, National Cancer Institute (INCA), located in Rio de Janeiro, Brazil.

The present study was submitted and approved by the Research Ethics Committee (CEP) of the respective institution under protocol nº 2.623.260 (CAE 85888318.1.0000.5274) and the informed written consent (IWC) was obtained through the signature of the patients or their legal guardians, after clarification on the objectives and procedures of the project by the researcher.

The exclusion criteria were: patients transferred from ICUs from other institutions; who were diagnosed with hepatic neoplasm; who did not have serum bilirubin results within 24 hours of ICU admission; who did not present with SIRS or sepsis; who presented histopathological report confirming benign tumor or that did not present diagnosis of neoplasia in histopathological report; who were readmitted to the ICU; who were dying within 48 hours of admission and those whose legal guardians or patients refused to sign the IWC.

2.2. Demographic and clinical data

Sociodemographic information and clinical data were obtained in physical and/or electronic medical records.

The use and the duration of the mechanical ventilation were followed during hospitalization in the units.

To calculate the length of hospital stay was considered the difference between the date of hospitalization until the date of discharge or death. In order to calculate the length of ICU stay, the difference between the date of ICU stay until discharge to the ICU ward or death was calculated.

The estimated morbidity and mortality, severity and prognosis of the disease were performed within 24 hours of ICU admission and calculated for each patient using the APACHE II (KNAUS et al., 1985) e SOFA I scores (VINCENT; MORENO; TAKALA, 1996).

2.3. mNUTRIC score

The mNUTRIC score was applied within 48 hours of ICU admission. The tool's total score ranges from zero to nine points. Patients with scores greater than or equal to five were classified as high nutritional risk and those who scored less than five were classified as low nutritional risk, according to the tool's information (RAHMAN et al., 2016).

2.4. Anthropometric evaluation

The information on weight and height were obtained in physical and/or electronic medical records within 48 hours of admission to the ICU. In the absence of this information in the medical records, the weight and height used corresponded to those indicated by guardians of the patients at the time of the interview (usual weight). The Body Mass Index (BMI) was obtained using the formula: weight (kg) / [height (m)]².

2.5. Biochemical parameters

Hematocrit (%), leukocytes (total/mm³), sodium (mmol/L), potassium (mmol/L), creatinine (mg/dL), platelets (thousand/ μ l) and total bilirubin (mg/dL) were collected from the medical records within 24 hours of admission and used to fill APACHE II and/or SOFA I. The values of C-Reactive Protein (mg/dL) and albumin (g/dL) were also collected within 24 hours of hospitalization in the ICU. Hypoalbuminemia was considered when albumin <3.5 g/dL (MCMILLAN, 2008).

2.6. Occurrence of death

Information on the occurrence of death was obtained through the physical and / or electronic medical record after 28 days of follow-up counted from the date of admission to the ICU.

2.7. Statistical analyzes

All the variables evaluated presented a non-normal distribution through the Kolmogorov-Smirnov test. Patients classified as high nutritional risk were compared with those with low nutritional risk according to the mNUTRIC score.

The simple descriptive analyzes presented the data in the form of tables, and the continuous variables were expressed through the median and interquartile range (IQR) and compared using the Mann-Whitney U test, while the categorical variables were expressed as percentage (%) and compared using the chi-square test.

Spearman's correlation was used to compare the mNUTRIC score and length of ICU stay (days), use of MV, age, C-Reactive Protein (CRP) and PS. As a classification of the degree of correlation, that is, of the force between the variables, the following parameter was used: when $0 < r < 0.4$; moderate when $0.4 < r < 0.7$ and strong when 0.7

$r < 1.0$ (SIQUEIRA; TIBURCIO, 2011). Correlations with statistical significance were those with $p \leq 0.05$ and degree of moderate or strong correlation.

Logistic regression was used to evaluate the association between the mNUTRIC score classification and outcomes with statistical significance in the chi-square test. Risk factors with statistical significance in univariate logistic regression were included in the multivariate regression analysis using the need for mechanical ventilation as a dependent variable and adjusted for sex and staging.

In all analyzes, the data collected were analyzed using IBM software, SPSS (IBM Corp., for Windows, version 22.0, Armonk, NY) and was adopted as statistical significance $p < 0.05$.

3. RESULTS

During the study period, 167 patients were admitted to the ICU of the respective institution and, after exclusion criteria, a total of 35 patients were included (**Figure 1**).

The general characteristics of the study participants are described in **Table 1**. The median age was 63 years (IQR 23-82), with a total of 51.4% of the male patients ($n=18$). The most prevalent tumor site was the gastrointestinal tract (35.5%), followed by tumors located in the head and neck (14.3%), haematological (11.4%), urinary system (8.6%) and tumors in other locations, which totaled 28.5%. Advanced staging and low functionality ($PS \geq 3$) were more prevalent in the study sample, accounting for 74.3% of the patients.

According to the mNUTRIC score instrument, 62.9% of these patients presented high nutritional risk.

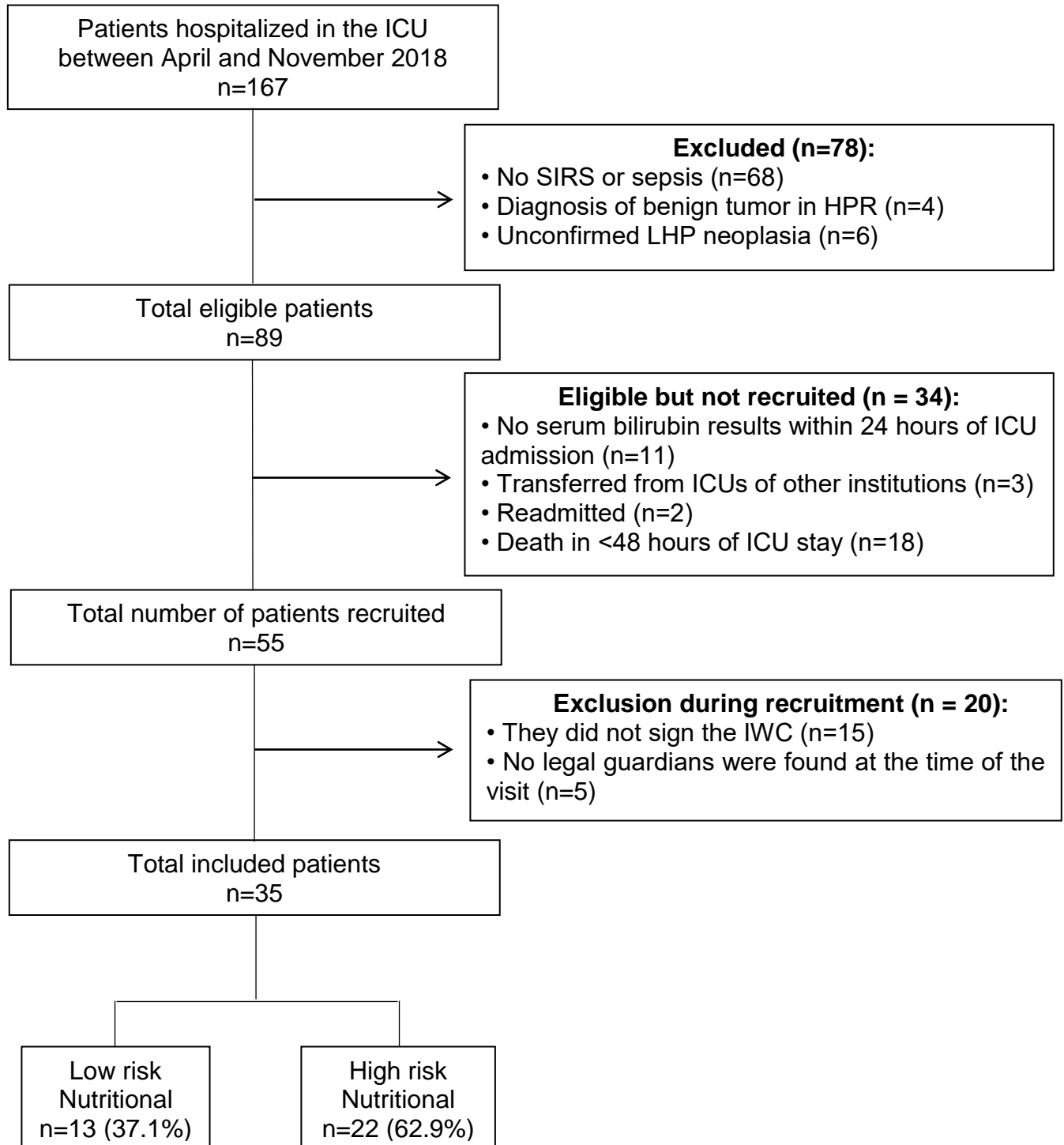


Figure 1 - Patients included in the research

ICU, Intensive Care Unit; SIRS, Systemic Inflammatory Response Syndrome; HPR, Histopathological report; IWC, Informed Written Consent.

Nutritional Risk Classification: according to the modified Nutrition Risk in the Critically ill (mNUTRIC score): Low nutritional risk mNUTRIC score <5; High Nutritional Risk: mNUTRIC score ≥5. Classificação do Risco Nutricional: de acordo com o *modified Nutrition Risk in the Critically ill* (mNUTRIC score): Baixo risco nutricional mNUTRIC score <5; Alto Risco Nutricional: mNUTRIC score ≥5.

Table 1 - Sociodemographic, clinical, severity and death characteristics according to the classification performed through the Modified Nutrition Risk in the Critically ill

Variables	Total (n=35)	Low NR (n=13)	High NR (n=22)	p value
Age (years)^c	63.0 [49.0–69.0]	52.0 [42.0–64.5]	63.5 [57.5–71.2]	0.021^{b*}
Gender^d				
Female	17 (48.6%)	7 (53.8%)	10 (45.5%)	0.631 ^a
Male	18 (51.4%)	6 (46.2%)	12 (54.5%)	
Site of tumor^d				
Digestive tract	13 (37.1%)	7 (53.8%)	6 (27.3%)	
Head and neck	5 (14.3%)	2 (15.4%)	3 (13.6%)	
Hematologic	4 (11.4%)	1 (7.7%)	3 (13.6%)	0.625 ^a
Urinary system	3 (8.6%)	0 (0.0%)	3 (13.6%)	
Other	10 (28.5%)	3 (23.1%)	7 (31.9%)	
Stages^d				
I/II	9 (25.7%)	1 (7.7%)	8 (36.4%)	0.185 ^a
III/IV	26 (74.3%)	12 (92.3%)	14 (63.6%)	
PS^d				
<3	9 (25.7%)	6 (46.2%)	3 (13.6%)	0.033^{a*}
≥3	26 (74.3%)	7 (53.8%)	19 (86.4%)	
MV^d				
Yes	23 (65.7%)	2 (15.4%)	21 (95.4%)	<0.001^{a*}
No	12 (34.3%)	11 (84.6)	1 (4.6%)	
mNUTRIC Score^c	5.0 [3.0–7.0]	2.0 [1.5–3.0]	6.0 [5.0–8.0]	<0.001^{b*}
APACHE II^c	25.0 [15.0–32.0]	14.0 [11.0–15.0]	29.5 [25.7–32.2]	<0.001^{b*}
SOFA I^c	9.0 [4.0–11.0]	3.0 [0.5–4.5]	10.0 [9.0–12.2]	<0.001^{b*}
BMI^c	23.9 [22.0–27.2]	24.3 [23.0–29.7]	23.5 [21.5–27.2]	0.564 ^b
Albumin (g/dL)^c	2.9 [2.5–3.3]	2.9 [2.8–3.6]	2.7 [2.4–3.3]	0.212 ^b
CRP (mg/dL)^c	12.7 [3.7–20.9]	9.2 [2.3–13.8]	14.6 [8.3–28.5]	0.026^{b*}
Hospital stay (days)^c	23.0 [15.0–30.0]	21.0 [13.5–27.5]	29.5 [18.0–30.2]	0.072 ^b
Length of ICU stay (days)^c	10.0 [6.0–21.0]	6.0 [2.5–7.5]	15.0 [10.0–23.2]	<0.001^{b*}
Death in 28 days^d	8 (22.9%)	2 (15.4%)	6 (27.3%)	0.101 ^a

^a Used chi-square test; ^bUsed Mann-Whitney U test; ^c Values expressed in Median [IQR (Q1-Q3)]; ^dAbsolute number (%); *statistical significance p <0.05.

IQR, Interquartile Range; NR, Nutritional Risk; PS, Performance Status; APACHE II, Acute Physiology and chronic health evaluation II; BMI, body mass index; CRP, C- Reative Protein; ICU, Intensive care unit; MV, Mechanical ventilation; SOFA I, Sequential organ failure assessment I; mNUTRIC score, modified Nutrition Risk in the Critically ill

At admission to the ICU, the median mNUTRIC score of the patients was 5.0 (IQR 3.0-7.0), the median APACHE II was 25.0 (IQR 15.0-32.0) and SOFA I of 9.0 (IQR 4.0-11.0) points. Regarding the use of MV, 65.7% of the patients needed this support. The median length of hospital stay was 23 days, ranging from at least eight days to at most 79 days, while the median length of ICU stay was 10 days (1-28). Patients who scored higher on the mNUTRIC score were older ($p=0.021$), had worse PS ($p=0.033$), higher CRP ($p<0.026$), had a greater need for MV use ($p<0.001$) consequently, they had longer ICU stay ($p<0.001$) (**Table 1**).

In **Table 2**, among the variables analyzed, the only use of MV presented a positive and significant correlation with the mNUTRIC score ($r=0.761$, $p<0.001$).

Table 2 – Correlation analysis between Modified Nutrition Risk in the Critically ill and clinical and prognostic variables (n = 35)

Variables	r	p value
Length of ICU stay (days)	0.574	<0.001
Age (years)	0.528	0.001
CRP	0.368	0.030
MV use (days)	0.761	<0.001

r, Spearman's rank correlation coefficient.

ICU, Intensive care unit; MV, Mechanical ventilation; CRP, C- Reative Protein; PS: *Performance Status*;
mNUTRIC score: *modified Nutrition Risk in the Critically ill*

Statistical significance $p < 0.05$.

The multivariate logistic regression model (adjusted for sex and staging) showed that those patients classified as high nutritional risk were 97.54 times more likely to use MV than those classified as low nutritional risk (CI 6.83 – 1391.71, $p = 0.001$) (**Table 3**).

Table 3 – Univariate and multivariate logistic regression (dependent variable: high nutritional risk)

Variable	Univariate			Multivariate*		
	OR	95% CI	p value	OR	95% CI	p value
MV use	115.50	9.39–1419.58	<0.001	97.54	6.83–1391.71	0.001

* adjusted for sex and staging

MV, Mechanical ventilation; mNUTRIC score: modified Nutrition Risk in the Critically ill; OR: Odds Ratio; 95% CI: Confidence Interval 95% for the relative risk.

Statistical significance $p < 0.05$.

4. DISCUSSION

This is the first study specifically evaluating critically ill cancer patients through the mNUTRIC score and its clinical outcomes at a referral brazilian hospital in oncology. In our study, we observed that the presence of high nutritional risk in critical cancer patients represents a decisive factor in its evolution, significantly increasing the need for invasive ventilation.

The median mNUTRIC score of this study was 5.0, being close to the value found in the validation study of this tool, which was 5.5 (RAHMAN et al., 2016). The classification of patients through the mNUTRIC score showed that 62.9% of the patients were at high nutritional risk (≥ 5 points). Similarly, Lee et al. (2018) and Chourdakis et al. (2018), when analyzing the results of their samples with patients of various pathologies, found 56% and 59% of patients as being at high nutritional risk, respectively.

Regarding age, patients at high nutritional risk were older when compared to those with low nutritional risk. Rahman et al.(2016) found very similar results when they found that there was a statistical difference between the groups of low nutritional risk and high nutritional risk, where the mean age in their sample was 65.9 years. Elderly are particularly vulnerable to malnutrition (BRABCOVÁ et al., 2016), due to biological, physiological, mental, social and economic risk factors (AHMED; HABOUBI, 2010; GIACALONE et al., 2016; HICKSON, 2006).

In this study, we did not find significant differences between high nutritional risk and mortality ($p = 0.101$). However, in relation to MV, we observed that those patients

with high nutritional risk presented 97.5 times more chances of utilization of MV when compared to those patients classified as low nutritional risk, with the model adjusted for sex and staging. Jeong et al (2018) evaluated patients with sepsis (46.3% of these patients had neoplasms), and found that 82.4% of patients at nutritional risk required MV. One of the explanations for this relationship is that malnutrition can compromise respiratory function, leading to muscle fatigue and acute respiratory failure (ARORA; ROCHESTER, 1982; KEENS et al., 1978).

The greater need for mechanical ventilation results in longer ICU stay (LOSS et al., 2015). According to the Second Brazilian Census of ICUs, the average time spent in intensive care units is one to six days (ORLANDO; MILANI, 2002). In our study, the median ICU length of hospital stay was ten days, but when we evaluated patients at high nutritional risk, the median time increased to 15 days. Corroborating our findings, Jeong et al. (2018) observed that patients with low nutritional risk (according to the NUTRIC score) had median time of stay in the ICU of 5 days while patients with high nutritional risk remained in the same for about 9 days.

We can then perceive that the critical patient is maintained for a prolonged period in these units, causing high financial costs (LOSS et al., 2015; MORITZ; SCHWINGEL; MACHADO, 2005), multiple colonizations by multiresistant microorganisms and malnutrition mainly in critical cancer patients due to the metabolic responses already presented due to the action of the tumor, aggressive antineoplastic treatment, stress caused by organic dysfunctions, use of innumerable drugs, immobilization, repeated interventions and other iatrogenic factors (SCHULMAN; MECHANICK, 2012), requiring actions that result in the reduction of the time spent in the ICU or the duration of the MV (DASTA et al., 2005).

One of the interventions proposed by Heyland et al.(2011) in creating the mNUTRIC score is that, in identifying a patient with a high nutritional risk, a more aggressive nutritional therapy, ie, adequacy of calories and proteins according to the recommendations, since these will have greater benefits when compared to those patients with low nutritional risk. Some recent studies have already shown a decrease in mortality with this intervention (HEYLAND et al., 2015; MUKHOPADHYAY et al., 2017; RAHMAN et al., 2016).

However, according to a recent guideline from the European Society for Clinical Nutrition and Metabolism (ESPEN), the mNUTRIC score presents as limitations the lack of classic nutritional variables (eg, BMI, weight loss, decrease in food intake) and, in addition, mortality is not the best outcome to evaluate the effectiveness of a nutritional intervention, considering the numerous factors that influence ICU mortality (SINGER et al., 2018). In this context, other forms of nutritional assessment, or specifically lean mass, such as ultrasonography, computed tomography or electrical bioimpedance (especially the obtaining of the phase angle) are indicated (DO AMARAL PAES et al., 2018; SINGER et al., 2018).

The main limitation of our study is the sample size and the different sites of tumor sites with different degrees of staging. To minimize this fact, the admission diagnosis in the ICU Units of Sepsis and SIRS was delimited as inclusion criteria.

5. CONCLUSÃO

We observed that the mNUTRIC score was effective as a predictor of worse clinical outcomes in critically ill cancer patients, such as the use of MV and longer ICU stay.

This instrument was clinically feasible for the initial use and identification of critically ill cancer patients who require early and specialized nutritional intervention in order to minimize the effects of the consequent functional disability.

However, further studies with a larger number of participants need to be conducted in this specific group of patients.

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