Modified Nutrition Risk in the Critically Ill (mNUTRIC) Score as a Prognostic Marker in Cancer Patients

Risco Nutricional Modificado nos Doentes Críticos (mNUTRIC) Pontuação como Marcador Prognóstico em Pacientes com Cancro

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Aline Pereira Pedrosa
Master in Clinical Nutrition, Federal University of Rio de Janeiro
Institute of Nutrition Josué de Castro (INJC), Health Sciences Center, Federal University of Rio de Janeiro, Rio de Janeiro, RJ
Av. Carlos Chagas Filho, 373, Health Sciences Center, Block J, 2nd Floor, Room 07
E-mail: alinepp.nut@gmail.com.

Wilza Arantes Ferreira Peres
PhD in Clinical Medicine, Federal University of Rio de Janeiro
Institute of Nutrition Josué de Castro (INJC), Health Sciences Center, Federal University of Rio de Janeiro, Rio de Janeiro, RJ
Av. Carlos Chagas Filho, 373, Health Sciences Center, Block J, 2nd Floor, Room 07
E-mail: wilza@nutricao.ufrj.br

Renata Brum Martucci
PhD in Food Science, Federal University of Rio de Janeiro
Department of Nutrition and Dietetics, Hospital do Cancer I, National Cancer Institute José Alencar Gomes da Silva (INCA), Rio de Janeiro, RJ
Praça da Cruz Vermelha, 23 – Centro – Rio de Janeiro – RJ
E-mail: renata.martucci@inca.gov.br

Livia Costa de Oliveira
PhD in Nutritional Science, Federal University of Rio de Janeiro
Department of Nutrition and Dietetics, Hospital do Cancer IV, INCA, Rio de Janeiro, RJ
R. Visc. de Santa Isabel, 274-A - Vila Isabel, Rio de Janeiro – RJ
E-mail: lillycostaoliveira@gmail.com

Tatiana Cathoud do Amaral Paes
Master in Clinical Nutrition, Federal University of Rio de Janeiro
Department of Nutrition and Dietetics, Hospital do Cancer I, National Cancer Institute José Alencar Gomes da Silva (INCA), Rio de Janeiro, RJ
Praça da Cruz Vermelha, 23 – Centro – Rio de Janeiro – RJ
E-mail: tcathoudpaes@gmail.com

ABSTRACT

Background: This study was aimed at evaluating the association of the Modified Nutrition Risk in the Critically Ill (mNUTRIC) Score with outcomes in critically ill cancer patients. *Methods:* It was an observational prospective cohort study in which the

patients were followed up for 28 days after their admission to the Intensive Care Unit (ICU). The logistic, linear regression models with negative binomial response and the Cox proportional hazards model were used to associate the mNUTRIC score and the outcomes. *Results:* Sixty patients were included in the study. Cancer patients who had higher values on the mNUTRIC score were older, showed worse performance status, a high C-reactive protein level, a greater need for the use of mechanical ventilation (MV), and stayed longer at the ICU. Additionally, cancer patients with a high nutritional risk were 134.9 times more likely to use MV, with an increase of 7.4 days in their ICU stay. No significant differences were found for not active cancer patients. Twenty-five percent of the patients died during the follow-up. *Conclusion:* The mNUTRIC score was effective as a predictor of the MV use and ICU length of stay in critical cancer patients. This instrument was capable of identifying patients who required an early nutritional intervention.

Keywords: critical care, neoplasms, nutrition assessment, prognosis

RESUMO

Antecedentes: Este estudo teve como objetivo avaliar a associação da pontuação de Risco Nutricional Modificado em Doentes Críticos (mNUTRIC) com resultados em pacientes com cancro em estado crítico. Métodos: Foi um estudo de coorte prospectivo observacional no qual os pacientes foram acompanhados durante 28 dias após a sua admissão na Unidade de Cuidados Intensivos (UCI). Os modelos de regressão logística e linear com resposta binomial negativa e o modelo de riscos proporcionais Cox foram utilizados para associar a pontuação mNUTRIC e os resultados. Resultados: Sessenta pacientes foram incluídos no estudo. Os pacientes com cancro que tinham valores mais elevados na pontuação mNUTRIC eram mais velhos, apresentavam pior estado de desempenho, um nível elevado de proteína C reactiva, uma maior necessidade de utilização de ventilação mecânica (VM), e permaneceram mais tempo na UCI. Além disso, os doentes com cancro com elevado risco nutricional tinham 134,9 vezes mais probabilidades de utilizar a VM, com um aumento de 7,4 dias na sua estadia na UCI. Não foram encontradas diferenças significativas para os doentes com cancro não ativos. Vinte e cinco por cento dos doentes morreram durante o seguimento. Conclusão: A pontuação mNUTRIC foi eficaz como preditor da utilização da VM e do tempo de internamento na UCI em pacientes com cancro em estado crítico. Este instrumento foi capaz de identificar os pacientes que necessitavam de uma intervenção nutricional precoce.

Palavras-chave: cuidados críticos, neoplasias, avaliação nutricional, prognóstico

1 INTRODUCTION

According to estimates by the National Cancer Institute José Alencar Gomes da Silva (INCA), in the triennium of 2020-2022, about 450 thousand new cases of cancer will rise in Brazil, except for non-melanoma skin cancer.[1] The relationship between malnutrition and cancer is well established in the literature, as it is the most common secondary diagnosis in these types of patients.[2] The nutritional status deficit in cancer can be explained by the release of several proinflammatory cytokines, such as interleukin 1, interleukin 6 (IL-6), tumor necrosis factor-alpha, interferon-alpha, and interferon-gamma,

which are produced by the tumor cells, which are responsible for protein and lipid catabolism[3,4], and the loss of appetite/decreased food intake. [5]

Individuals with malignant diseases have been increasingly admitted to Intensive Care Units (ICUs), occupying about 18% of the beds.[6] Recent studies show that patients with active cancer and sepsis have a higher mortality rate at a 28-day follow-up period compared to patients without cancer.[7,8] In addition, 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 treatment, the quality of life, and functional capacity, increasing the risk of infections, hospitalization time, and death occurrence.[9] However, no data was found regarding the association between nutritional risk, critical illness and cancer.

The nutritional assessment in critically ill patients is a challenge, since the traditional tools to assess the degree of malnutrition in these patients are limited[10], due to metabolic and hydration alterations, bed restrictions, and the need for mechanical ventilation (MV) or sedation that may change the level of consciousness.[11-13] Heyland et al.[14] developed the Nutrition Risk in the Critically Ill (NUTRIC) Score, a specific score for critically ill patients. This tool considers parameters, such as the 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 the ICU admission, and IL-6. Subsequently, a modified Nutrition (mNUTRIC) Score was proposed, excluding IL-6 of the parameters considered.[15] According to this tool, patients classified with a high nutritional risk (mNUTRIC score ≥5) are more prone to worse clinical outcomes.[16] The metric score was validated by Rahman et al. (15) and then translated into Portuguese by Mendes et al.[16]

Currently, many studies[17-20] have been conducted when using the mNUTRIC score as a tool for a nutritional assessment and in screening critically ill patients; however, its applicability in cancer patients needs to be studied. Thus, the objective of this study was to associate the mNUTRIC score with the clinical outcomes of critically ill cancer patients.

2 METHODS

2.1 STUDY POPULATION

This was an observational prospective cohort study, carried out between April and November 2018 with active cancer and not active cancer patients admitted to the ICU of

a referral hospital in oncology, who were then followed up for 28 days. This study was approved by the Research Ethics Committee of the institution (N. 2.623.260), and the patients or their legal guardians signed the Informed Consent Form (ICF). The design and the analysis were performed according to the STROBE statement.[21]

The study included male and female individuals, ≥20 years old, who were diagnosed with a systemic inflammatory response syndrome (SIRS), sepsis or septic shock. The exclusion criteria were: patients transferred to the ICU from other ICU institutions; those who were diagnosed with hepatic neoplasm; those who did not present SIRS or sepsis; those who were readmitted to the ICU; those who died within 48 hours of admission; those whose legal guardians or patients refused to sign the ICF; and those who did not have serum bilirubin results within 24 hours of their ICU admission.

2.2 DEMOGRAPHIC AND CLINICAL DATA

The sociodemographic information (age and gender) and clinical data were obtained from the medical records (site of the tumor, stage, and performance status). The tumor stage was defined as initial or advanced, preferably by the clinical stage and the TNM system (primary tumor, regional lymph nodes, and distant metastasis) classification, depending on the tumor. The initial stage was considered as in situ (Tis or stage 0); localized extension; stage I–II; TNM T1–2, N0, and M0; or histologic grade 1 (well-differentiated) and 2 (moderately well-differentiated). The advanced stage was considered as regional or distant extension; stage III-IV; TNM T3–4, N1–3, and M1; or histologic grade 3 (poorly differentiated), and 4 (undifferentiated).[22] Four patients with leukemia and myeloma remained without any stages (11.4%).

Active cancer patients were those currently undergoing curative or palliative chemotherapy, radiotherapy, immunotherapy or surgery.[23] Not active cancer patients were considered to be those who had a negative histopathological examination for cancer and / or those who, in the past, where diagnosed with cancer but are currently free of the disease after undergoing treatment.[24] SIRS was considered when two or more criteria were met: temperature >38ºC or <36ºC; heart rate >90/min; respiratory rate >20/min or $PaCO_2$ <32 mmHg; white blood cell count >12000/mm³ or <4000/mm³ or >10% immature bands.[25] Sepsis was defined as infection or suspected infection plus a ≥2-point increase in the SOFA score. Infection or suspected infection was defined as follows: 1) any of the following term in the patient's medical record according to the Ninth Revision of the International Classification of Diseases: "infection", "pneumonia", "meningitis",

"peritonitis", "bacteremia", "sepsis" or "septic" and 2) a positive microbiological culture.[26] Patients with septic shock were identified with a clinical construct of sepsis with persisting hypotension requiring vasopressors to maintain mean arterial pressure ≥65 mmHg and having a serum lactate level >2 mmol/L (18 mg/dL), despite adequate volume resuscitation.[27]

Information about the use and the duration of MV were followed during the hospital admission to the ICU.

In order to calculate the length of the hospital stay, this was considered as the difference between the date between hospital admission and discharge or death. To calculate the length of the ICU stay, the difference between the date of the ICU stay until discharge to the ICU ward or death was considered.

2.3 THE MNUTRIC SCORE

The mNUTRIC score was applied within 48 hours of the ICU admission. The tool's total score ranged from zero to nine points. Those patients with scores greater than or equal to five were classified as with a high nutritional risk, and those who scored less than five were classified as of low nutritional risk, according to the tool's information.[15]

2.4 ANTHROPOMETRIC EVALUATION

The information on weight and height was obtained from the medical records within 48 hours of admission. In the absence of this information, the weight and height used corresponded to those figures indicated by the legal guardians of the patients (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), and potassium (mmol/L) were used to fill APACHE II.[28] The platelets (thousand/µl), and total bilirubin (mg/dL) were used to fill SOFA I.[29] The creatinine (mg/dL) were collected to fill APACHE II[27] and SOFA I.[29] In addition, the values of C-reactive protein (CRP) (mg/dL) and albumin (g/dL) were also collected. Hypoalbuminemia was considered when albumin <3.5 g/dL.[30] All biochemical parameters were collected from the medical records within 24 hours of the patient's admission to the ICU.

2.6 OCCURRENCE OF DEATH

Information on the occurrence of death was obtained through medical records. Survival time was calculated from the date of the ICU stay until death or to the end of the follow-up (28 days).

2.7 STATISTICAL ANALYSIS

The Kolmogorov-Smirnov test was performed to assess the distribution symmetry. The continuous variables were expressed through the median and the interquartile range (IQR), and they were compared using the Mann-Whitney U test; the categorical variables were expressed as percentages (%) and were compared using the Chi-squared test (X^2). The variables with a statistical significance ($p<0.20$) between the nutritional risk were included in the correlation analyses.

Spearman's correlation was used to relate the mNUTRIC score and clinical outcomes. As a classification of the degree of correlation, it was weak when $0 < r < 0.4$, moderate when $0.4 < r < 0.7$, and strong when $0.7 < r < 1.0$.[31]

The regressions were used when the correlation analysis showed $p<0.05$ and/or with a moderate or strong correlation. Thus, the logistic regression was used to evaluate the association between the mNUTRIC score and the use of MV (yes/no). Linear regression models with negative binomial response were used to evaluate the association between the mNUTRIC score with ICU stay (days). Survival was analyzed by the Kaplan-Meier curve and the log-rank test, and logistic regression analyses were performed using the Cox proportional hazards model.

In all analyses, the data collected was analyzed when using IBM software, SPSS (IBM Corp., for Windows, Version 22.0, Armonk, NY), and a statistical significance of $p < 0.05$ was adopted.

3 RESULTS

During the period considered, 182 patients were admitted to the ICU and, after the exclusion criteria, 60 of them were included in the study**.** Of these, 35 patients had active cancer and 25 patients did not have active cancer (**Figure 1**). [Figure 1 near here]

Median age was 67 (61─75) years. An advanced cancer stage and low functionality were extremely prevalent, representing 71% and 82% of the patients respectively. Most cancer and not active cancer patients presented a high nutritional risk (63% and 76% respectively); 66% and 88% of the cancer and not active cancer patients

needed MV respectively. Active cancer patients with a high mNUTRIC score were older (p=0.021), had a worse PS (p=0.033), a higher CRP (p=0.026), and a greater need for the use of MV (p<0.001); consequently, they stayed longer at the ICU (p<0.001), while patients without active cancer and with a high mNUTRIC score were older (p=0.028) and had a longer hospital stay (p=0.035). Seven patients with active cancer (20%) and eight patients without active cancer (32%) died during the 28-day follow-up (**Table 1**). [Table 1 near here] The survival of active cancer patients who were classified as a high nutritional risk was lower when compared to the patients with a low nutritional risk, being 72.7% and 92.3% respectively. However, there were no statistical differences in the survival of the groups (p=0.182) and, according to the Cox proportional hazards model, mNUTRIC was not considered an independent prognostic factor [data not shown].

Among patients with active cancer, the most prevalent tumor site was the gastrointestinal tract (35.5%), followed by tumors that were located in the head and neck (14.3%). Most of them have an advanced stage of the disease (71.4%) (Table 2). [Table 2 near here]

Table 3 shows that the variable lengths of the ICU stay (days) and age (years) presented a moderate correlation with the mNUTRIC score both in cancer patients (r=0.574; p<0.001 and r=0.528; p=0.001 respectively) and in patients without active cancer (r=0.566; p=0.003 and r=0.657 and p<0.001). Additionally, the PS also showed a moderate correlation in patients without active cancer (r=0.525; p=0.007), which was not statistically significant in patients with cancer (r=0.301; p=0.079). However, the use of MV (days) was the only one with a strong correlation with the instrument mentioned in cancer patients (r=0.761; p< 0.001) [Table 3 near here]. When observing not active cancer patients, no variable had a strong correlation with the mNUTRIC score. Regarding the impact of cancer treatment on clinical outcomes, we did not find statistical differences (Table 4). [Table 4 near here]

Cancer patients with a high nutritional risk had an increased risk of the use of MV (OR 134.9; 95% CI 6.6─2,751.1) and had an increase of 7.4 days in the ICU stay (95% CI 1.8─13.0) when compared with those with a low nutritional risk (Table 5 and Table 6). [Table 5 near here]. For each point of the mNUTRIC score, there was a greater risk of the use of MV (OR 9.3; 95% CI 2.9─29.0) and an increase of 1.5 days in the ICU stay (95% CI 0.1─2.9) (Table 6). [Table 6 near here] No significant results were found for not active cancer patients both for the use of MV and for ICU stay (Table 5 and Table 6).

4 DISCUSSION

As far as the authors are concerned, this is the first study to evaluate critically ill cancer patients through the mNUTRIC score and its clinical outcomes in an ICU, conducted in a reference oncology center. In this study, the researchers noticed that the presence of a high nutritional risk in critical cancer patients represented a decisive factor in their evolution, mainly increasing the need for MV and the length of the ICU stay. This was not observed in patients without active cancer, demonstrating the predictive power of the tool in patients with active cancer.

The median mNUTRIC score in this study was 6, being close to the value found in the validation study of this tool, which was 5.5.[15] The classification of patients through the mNUTRIC score showed that 63% and 76% of the patients with active cancer and without active cancer were at a high nutritional risk. Similarly, Lee et al.[17] and Chourdakis et al.[19], when analyzing the results of their samples with patients with various pathologies, found 56% and 59% of patients at a high nutritional risk respectively.

Regarding age, in patients with active cancer and in those without active cancer, the patients at a high nutritional risk were older when compared to those with a low nutritional risk. Rahman et al.[15] found remarkably similar results when they determined that there was a statistical difference between the groups at low nutritional risk and at a high nutritional risk, where the mean age in their sample was 65.9 years. The elderly are particularly vulnerable to malnutrition[32], due to biological, physiological, mental, social, and economic risk factors.[33-35]

When the present study analyzed the correlation of the stage of the tumor with the mNUTRIC score, the researchers realized that there was an inverse relationship, that is, the larger the mNUTRIC score, the smaller the stage, although this relationship did not show a statistical difference. Brun-Buisson et al.[36] studied the characteristics of critical oncology patients and they observed that the patients with solid tumors had a similar severity and general profiles close to the not active cancer population. This was different from hematologic patients, who showed more diagnosis of sepsis than those patients without active cancer. As this study had a larger sample of patients with solid tumors (88.6%), this relationship was extrapolated in this study. That is, when the patient with solid tumors was admitted to the ICU, the severity of the critical condition was more important than the stage of the tumor.

In this study, death rates of 20% and 32% were observed in active cancer patients and in patients without active cancer respectively, and significant differences between a

high nutritional risk and mortality were not found in both groups (p=0.220 and p=0.054 respectively). In the NUTRIC score development study[14], and in the validation of the mNUTRIC score[15], they used the same follow-up time as in this study (28 days) and they observed a similar mortality of 23% and 29% respectively. Corroborating these findings, Mukhopadhyay et al.[37] also observed 21.7% of death during the 28-day follow-up period. Other studies, with a follow-up ranging from 60 to 360 days, found mortality rates between 15% and 29%.[17, 19, 38] Do Amaral Paes et al.[38] performed a prospective observational study with 31 critical cancer patients and they observed 29% of death in one year.

Studies comparing cancer patients and cancer-free control patients have shown that cancer patients have higher mortality rates when admitted to ICUs.[7,8] Dagher et al.[7] compared the clinical outcomes of 176 cancer patients and 176 cancer-free controls who had sepsis, septic shock or bacteraemia, and showed that critical cancer patients had 2.320 (CI 95% 1.225 to 4.395, p=0.010) odds of dying compared with those without cancer in the setting of sepsis. Corroborating these results, Wang et al.[8] analyzed 22,382 cancer-free patients and 1,574 active cancer patients (all with concomitant diagnosis of sepsis) and observed a mortality rate of 63% in active cancer patients and of 36.5% in cancer-free patients (p<0.001). In this study, we find did not find statistical differences in the mortality of patients with active cancer and without active cancer, probably due to the small sample. Besides that, we may have possibly found a lower mortality rate in active cancer patients of this study because 42.9% of the sample did not have sepsis, being classified as SIRS. In not active cancer patients, only 24.0% had SIRS and possibly because of this fact they showed a higher mortality rate when compared to patients with active cancer, although it was not statistically significant (p=0.290). According to The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3), SIRS should not be a criterion to identify patients with sepsis because it does not indicate dysregulated, life-threatening response.[27] This syndrome is present in many hospitalized patients, including those who never develop infection and never have adverse outcomes.[39]

In this study, CRP was increased in active cancer patients with a high nutritional risk, with a median of 15 mg/dL and, although it had a weak correlation with the mNUTRIC score, it presented statistical differences between the groups with high and low nutritional risk (p=0.030), demonstrating the importance of a CRP evaluation as an associated variable of nutritional risk in this specific population. In not active cancer patients, there were no statistical differences between patients with high and low

nutritional risk (p=0.525). The difference in these findings between cancer and not active cancer patients can be explained because cancer patients have increased CRP, probably a secondary response to tumor necrosis, local tissue damage, and associated inflammation in patients with neoplasms.[40]

In the development of the NUTRIC score tool, Heyland et al.[14] observed that CRP and procalcitonin had no association with mortality, or their inclusion did not improve the fit to the final model. Thus, when IL-6 is not available, it should be excluded from the score, because there is no advantage in replacing IL-6 with CRP. In contrast, another study compared the NUTRIC score when using IL-6 and the same tool, replacing IL-6 for CRP. The authors concluded that the CRP incorporation increased the performance of this score, and it could replace IL-6 when this substance is not available.[41] To evaluate the inflammatory state, the dosage of CRP is recommended every 24 hours, in order to identify new infections in patients, especially those at a high risk of infection (MV, airway aspiration, central vascular catheter).[42]

Regarding MV, active cancer patients with a high nutritional risk presented 134.9 times more chance to use MV when compared to those patients who were classified as having low nutritional risk, with the model adjusted for age, gender, cancer stage, and CRP. No statistical differences were found in not active cancer patients (p=0.185). The rate of MV in patients with solid cancer range from 54 to 74%[43,44] and recent studies reported that the incidence of prolonged MV among cancer patients is 10.4 per 100 ICU admissions.[45] Jeong et al.[20] evaluated patients with sepsis (46.3% of them had neoplasms) and they found that 82.4% of the patients with nutritional risk required MV. One of the explanations for this is the relationship between inflammation and nutritional status. A recent study has shown that cancer patients with higher serum CRP values have worse nutritional status.[46] Consequently, malnutrition compromises the respiratory function, leading to muscle fatigue and acute respiratory failure.[47,48] In addition, the small sample of this study may have impacted the results.

The need for MV results in a longer ICU stay is greater.49. According to Orlando and Millani (2013), the average time spent in intensive care units is from one to 6 days.[50] In this study, the average ICU length of hospital stay was 10 days for active cancer patients, but when the patients at a high nutritional risk were evaluated, the average time increased to 15 days, and at each point of the mNUTRIC score, it increased by 7.4 days in the ICU stay. Corroborating the findings of the current study, Jeong et al.[20] observed that patients with a low nutritional risk (according to the NUTRIC score) had an average

time of stay in the ICU of 5 days, while patients with a high nutritional risk remained in the ICU for about 9 days.

It can then be noticed that critically ill cancer patients are maintained for a longer period in these units, causing high financial costs[49, 51], and multiple colonization by multiresistant microorganisms and malnutrition, due to the action of the tumor. This increases the stress that is caused by organic dysfunctions, the use of various drugs, immobilization, repeated interventions, and other iatrogenic factors, quickly leading to malnutrition[52], requiring specialized nutritional therapy. Consequently, this reduces the time spent in the ICU or in the duration of the MV.[53]

One of the interventions proposed by Heyland et al.[14] was the creation of the mNUTRIC score as a way of identifying a patient with a high nutritional risk, together with employing a more aggressive nutritional therapy. In other words, an adequacy of calories and proteins according to the recommendations will have greater benefits when compared to those patients with a low nutritional risk. Some recent studies have already shown a decrease in mortality with this type of intervention.[15, 37, 54]

However, according to recent guidelines from the European Society for Clinical Nutrition and Metabolism (ESPEN), the mNUTRIC score presents as limitation a lack of classic nutritional variables; for instance, BMI, weight loss, and food intake decrease. In addition, mortality is not the best outcome to evaluate the effectiveness of a nutritional intervention when considering the numerous factors that influence the ICU mortality[54]. In this context, other forms of nutritional assessment, or specifically, lean mass, such as ultrasonography, computed tomography, or electrical bioimpedance (especially the measurement of the phase angle) are suggested.[38, 55]

The main limitations of this study were the small sample size and the different types of tumor sites and histology, together with different degrees of cancer stage. To minimize these facts, the admission diagnosis in the ICU and the units of sepsis, septic shock and SIRS were delimited as inclusion criteria. In our study, it was also not possible to compare the clinical outcomes of active cancer patients with cancer-free patients because the sample consisted only of active and not active cancer patients, and the study was conducted at a referral cancer treatment hospital.

5 CONCLUSIONS

In active cancer patients, we observed that the mNUTRIC score was effective as a predictor of worse clinical outcomes in critically ill cancer patients, such as in the use

of MV and a longer ICU stay. In addition, the CRP values were significantly higher in those with a high nutritional risk and they could be used concomitantly with the mNUTRIC score.

This instrument was clinically feasible for the initial use and the identification of critical cancer patients who required early and specialized nutritional interventions, in order to minimize the effects of consequent functional disability.

Our study, therefore, demonstrates that worse nutritional status could increase the occurrence of adverse outcomes in the critical cancer population (which already has worse clinical outcomes). However, further studies with a larger number of participants need to be conducted in this specific group of patients.

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ANEXOS

Table 1. Sociodemographic, clinical, severity, and death characteristics of active and not active cancer patients, according to the classifications performed through the modified Nutrition Risk in the Critically Ill.

Variables	Total (n=60; 100%)	Active Cancer Patients (A)[f]				Not Active Cancer Patients (B)[g]				A vs B[e]
		Total (n=35; 58%)	Low NR (n=13; 37%)	High NR (n=22; 63%)	p-value	Total (n=25; 42%)	Low NR (n=6; 24%)	High NR (n= 19; 76%)	p-value	p-value
Age (years)[b,c]	67 [61─75]	63 [49─69]	52 [42─64]	63 [57─71]	**0.021***	64 [58─71]	59 [54─61]	67 [61─75]	**0.028***	0.251
Gender[a,d]										
Female	30 (50%)	17 (49%)	7 (54%)	10 (46%)		13 (52%)	3 (50%)	10 (53%)	0.910	0.793
Male	30 (50%)	18 (51%)	6 (46%)	12 (54%)	0.631	12 (48%)	3 (50%)	9(47%)		
SIS[a,d]										
SIRS	21 (35%)	15 (43%)	7 (54%)	8 (36%)		6 (24%)	4 (66%)	2 (10%)		
Sepsis	28 (47%)	16 (46%)	6 (46%)	10 (46%)	0.229	12 (48%)	1 (17%)	11 (58%)	**0.019***	**<0.001***
Septic shock	11 (18%)	4 (11%)	0	4 (18%)		7 (28%)	1 (17%)	6 (32%)		
PS[a,d]										
<3	11 (18%)	9 (26%)	6 (46%)	3 (14%)	**0.033***	2 (8%)	0	2 (10%)	0.407	0.080
≥3	49 (82%)	26 (74%)	7 (54%)	19 (86%)		23 (92%)	6 (100%)	17 (90%)		
MV[a,d]										
Yes	45 (75%)	23 (66%)	2 (15%)	21 (95%)	**<0.001***	22 (88%)	6 (100%)	16 (84%)	0.299	**0.049***
No	15 (25%)	12 (34%)	11 (85%)	1 (5%)		3 (12%)	0	3 (16%)		

mNUTRIC Score[c]	6 [3─7]	5 [3─7]	2 [1─3]	6 [5─8]	**<0.001***	7 [4─8]	3 [2─3]	7 [6─8]	**<0.001***	**0.037***
APACHE II[b,c]	26 [15─32]	25 [15─32]	14 [11─15]	29 [26─32]	**<0.001***	29 [23─33]	21 [13─28]	29 [26─33]	0.116	0.164
SOFA I[b,c]	9 [5─12]	9 [4─11]	3 [1─4]	10 [9─12]	**<0.001***	12 [8─15]	8 [0─16]	12 [9─14]	0.298	**0.031***
BMI (kg/m²)[b,c]	24 [22─28]	24 [22─27]	24 [23─29]	23 [21─27]	0.564	24 [22─28]	24 [23─31]	24 [22─28]	0.703	0.902
Albumin (g/dL)[b,c]	3 [2─3]	3 [2─3]	3 [3─4]	3 [2─3]	0.212	3 [2─3]	3 [2─3]	3 [2─3]	0.774	0.594
CRP (mg/dL)[b,c]	12 [4─26]	13 [4─21]	9 [2─14]	15 [8─28]	**0.026***	10 [4─28]	9 [3─28]	11 [5─28]	0.525	0.910
Hospital stay (days)[b,c]	28 [19─31]	23 [15─30]	21 [13─27]	29 [18─30]	0.072	30 [23─40]	34 [31─85]	29 [12─33]	**0.035***	**0.045***
ICU stay (days)[b,c]	12 [6─22]	10 [6─21]	6 [2─7]	15 [10─23]	**<0.001***	17 [6─25]	24 [4─28]	14 [7─22]	0.503	0.251
Death in 28 days[a,d]	15 (25%)	7 (20%)	1 (8%)	6 (27%)	0.220	8 (32%)	0	8 (42%)	0.054	0.290

a Chi-square test; b Mann-Whitney U test; c Median [IQR (Q1-Q3)]; d Absolute number (%); eComparison of total active cancer and total not cancer patients according to the selected variables; fActive cancer patients were those currently undergoing curative or palliative chemotherapy, radiotherapy, immunotherapy or surgery. gNot active cancer patients were considered to be those who had a negative histopathological examination for cancer and / or those who, in the past, where diagnosed with cancer but are currently free of the disease after undergoing treatment. [1]Patients with myeloma or leukemia. IQR: interquartile range; NR: nutritional risk; PS: Performance Status; APACHE II: Acute Physiology and Chronic Health Evaluation II; BMI: body mass index; CRP: C-reactive protein; ICU: intensive care unit; MV: mechanical ventilation; SOFA I: Sequential Organ Failure Assessment I; mNUTRIC: modified Nutrition Risk in the Critically Ill; ; Low Nutritional Risk mNUTRIC Score <5; High Nutritional Risk: mNUTRIC Score ≥5; SIS: Systemic Inflammatory Syndromes; SIRS: Systemic Inflammatory Response Syndrome. *statistical significance p <0.05

Table 2. Clinical characteristics of active cancer patients, according to the classifications performed through the modified Nutrition Risk in the Critically Ill.

Variables	Total (n=35)	Active Cancer Patients[c] (n=35; 58.3%)		p-value
		Low NR (n=13; 37.1%)	High NR (n=22; 62.9%)	
Site of tumor [a,b]				
Digestive tract	13 (37.1%)	7 (53.8%)	6 (27.3%)	0.625
Head and neck	5 (14.3%)	2 (15.4%)	3 (13.6%)	
Hematologic	4 (11.4%)	1 (7.7%)	3 (13.6%)	
Urinary system	3 (8.6%)	0	3 (13.6%)	
Other	10 (28.6%)	3 (23.1%)	7 (31.9%)	
Stages [a,b]				
I/II	6 (17.2%)	1 (7.7%)	5 (22.7%)	0.185
III/IV	25 (71.4%)	11 (84.6%)	14 (63.7%)	
Without Stages[1]	4 (11.4%)	1(7.7%)	3 (13.6%)	
Cancer treatment [a,b]				
Surgery	28 (80.0%)	13 (100.0%)	15 (68.2%)	0.160
Chemotherapy	2 (5.7%)	0	2 (9.1%)	
Radiotherapy	2 (5.7%)	0	2 (9.1%)	
No treatment	3 (8.6%)	0	3 (13.6%)	

[a]Active cancer patients were those currently undergoing curative or palliative chemotherapy, radiotherapy, immunotherapy or surgery. [b]Not active cancer patients were considered to be those who had a negative histopathological examination for cancer and / or those who, in the past, where diagnosed with cancer but are currently free of the disease after undergoing treatment. R: Spearman's rank correlation coefficient. PS: Performance Status; CRP: C- reactive protein; ICU: intensive care unit; MV: mechanical ventilation; *Statistical significance p <0.05.

Table 4. Correlation analysis between cancer treatment (chemotherapy, radiotherapy, surgery and no treatment) and the clinical outcomes (n=35)

Cancer Treatments	Active Cancer[a] (n=35; 58.3%)							
	MV (yes/no)		Length of ICU stay (days)		Hospital stay (days)		Death in 28 days (yes/no)	
	R	p-value	R	p-value	R	p-value	R	p-value
Chemotherapy	-0.068	0.700	0.144	0.410	0.106	0.545	0.089	0.612
Radiotherapy	-0.180	0.300	0.128	0.463	-0.081	0.643	0.272	0.114
Surgery	-0.261	0.063	0.322	0.059	0.124	0.477	0.286	0.096
No treatment	0.221	0.202	-0.278	0.105	-0.198	0.254	-0.102	0.560

[a]Active cancer patients were those currently undergoing curative or palliative chemotherapy, radiotherapy, immunotherapy or surgery; R: Spearman's rank correlation coefficient. ICU: intensive care unit; MV: mechanical ventilation; *Statistical significance p <0.05.

Table 5. Multivariate logistic regression between the modified Nutrition Risk in the Critically Ill and MV use (yes/no).

	Active Cancer[a] (n=35; 58.3%)			Not Active Cancer[b] (n=25; 41.7%)		
	OR	95% CI	p-value	OR	95% CI	p-value
mNUTRIC score (Total)	9.3	2.9-29.0	**0.001***	3.2	0.8-11.2	0.098
Low NR	1	-	-	1	-	-
High NR	134.9	6.6–2,751.1	**0.001***	5.4	0.9-9.4	0.185

Adjusted for age, gender, cancer stage and CRP;
[a]Active cancer patients were those currently undergoing curative or palliative chemotherapy, radiotherapy, immunotherapy or surgery. [b]Not active cancer patients were considered to be those who had a negative histopathological examination for cancer and / or those who, in the past, where diagnosed with cancer but are

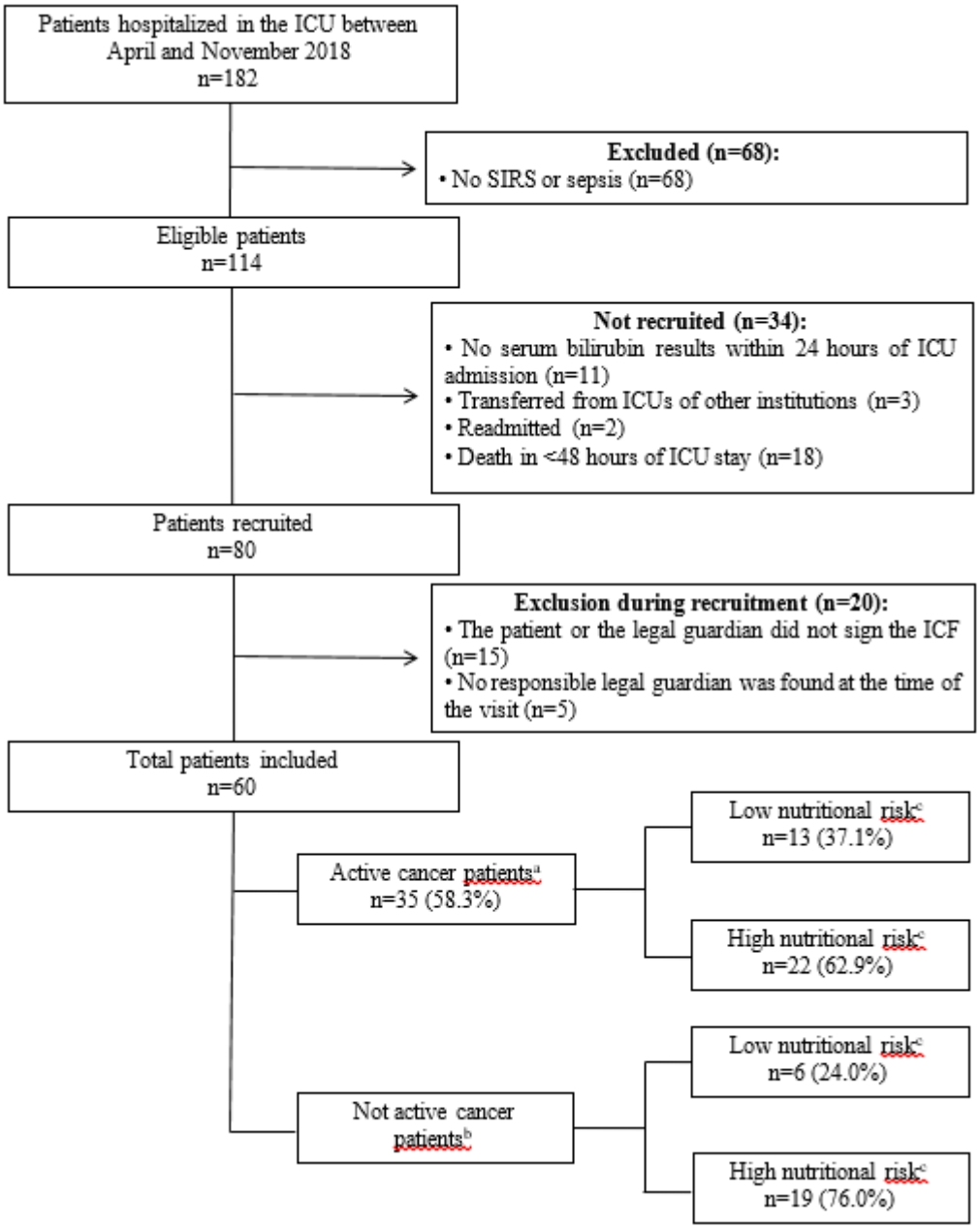
currently free of the disease after undergoing treatment. *Statistical significance p <0.05. CI: confidence interval; MV: mechanical ventilation; mNUTRIC: modified Nutrition Risk in the Critically Ill; Low Nutritional Risk mNUTRIC Score <5; High Nutritional Risk: mNUTRIC Score ≥5; OR: odds ratio.

Table 6. Multivariate linear regression models with negative binomial response between the modified Nutrition Risk in the Critically Ill and Length of ICU stay (days).

	Active Cancer[a] (n=35; 58.3%)			**Not Active Cancer[b] (n=25; 41.7%)**		
	β	**95% CI**	**p-value**	**β**	**95% CI**	**p-value**
mNUTRIC score (Total)	1.5	0.1-2.9	0.040*	1.4	0.3-3.1	0.102
Low NR	1	-	-	1	-	
High NR	7.4	1.8-13.0	0.010*	5.6	-4.4-15.6	0.276

Adjusted for age, gender, cancer stage and CRP;
[a]Active cancer patients were those currently undergoing curative or palliative chemotherapy, radiotherapy, immunotherapy or surgery. [b]Not active cancer patients were considered to be those who had a negative histopathological examination for cancer and / or those who, in the past, where diagnosed with cancer but are currently free of the disease after undergoing treatment. *Statistical significance p <0.05.
β: linear regression coefficient; CI: confidence interval; ICU: intensive care unit; mNUTRIC: modified Nutrition Risk in the Critically Ill; Low Nutritional Risk mNUTRIC Score <5; High Nutritional Risk: mNUTRIC Score ≥5.

Figure 1. Patients included in the research



[a] Active cancer patients were those currently undergoing curative or palliative chemotherapy, radiotherapy, immunotherapy or surgery. [b] Not active cancer patients were considered to be those who had a negative histopathological examination for cancer and/or those who, in the past, were diagnosed with cancer but are currently free of the disease after undergoing treatment. [c]modified Nutrition Risk in the Critically Ill (mNUTRIC) Score: Low Nutritional Risk mNUTRIC Score <5; High Nutritional Risk: mNUTRIC Score ≥5. ICU: Intensive Care Unit; SIRS: Systemic Inflammatory Response Syndrome; HPR: Histopathological report; ICF: Informed Consent Form.