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ARÁN

Nutrición Hospitalaria

Trabajo Original

Valoración nutricional

The appearance of malnutrition in hematological inpatients prolongs hospital stay: the need for nutritional surveillance during hospitalization

La aparición de desnutrición en el paciente hematológico ingresado alarga la estancia: la necesidad de vigilancia nutricional en el ingreso

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Abstract

Introduction: oncohematological diseases are associated with a high prevalence of malnutrition during hospitalization. Our aim was to analyze the appearance and repercussions of malnutrition in well-nourished hematological inpatients at admission.

Method: a prospective one-year study conducted in hematology inpatients. The Malnutrition Screening Tool (MST) was used at admission and repeated weekly. Patients with a negative screening at admission who developed malnutrition during hospitalization constituted our study sample. A nutritional evaluation and intervention was performed. We also analyzed the effect of newly diagnosed malnutrition on patients' outcomes in comparison with the outcomes of patients that remained well-nourished during hospitalization.

Results: twenty-one percent of hematological inpatients who were well nourished at admission developed malnutrition during hospitalization. Of the patients, 62.4% needed a nutritional intervention (100% oral supplements, 21.4% diet changes, 5.2% parenteral nutrition). After intervention, an increase in real intake was achieved (623 kcal and 27.3 g of protein/day). Weight loss was slowed and visceral protein was stabilized. Length of stay was 8.5 days longer for our sample than for well-nourished patients.

Conclusions: newly diagnosed malnutrition appeared in one in five hematological well-nourished inpatients, leading to a longer length of stay. Nutritional intervention improved intake and nutritional status. Nutritional surveillance should be mandatory.

Key words:

Hematological neoplasms. Nutrition assessment. Nutritional status. Malnutrition. Energy intake.

Resumen

Introducción: las enfermedades oncohematológicas asocian una elevada prevalencia de malnutrición, especialmente durante la hospitalización.

Objetivo: analizar la aparición de malnutrición y su repercusión en pacientes normonutridos al ingreso.

Métodos: estudio prospectivo de un año en una cohorte de ingresados hematológicos. El Malnutrition Screening Tool (MST) se realizó al ingreso, repitiéndose semanalmente. Los pacientes con cribado negativo al ingreso que desarrollaron malnutrición durante la hospitalización constituyeron nuestra muestra. Se realizó evaluación e intervención nutricional, analizando el efecto de la aparición de malnutrición en el pronóstico, comparado con los pacientes que permanecieron normonutridos.

Resultados: el 21% de los pacientes normonutridos al ingreso desarrolló malnutrición en la hospitalización. El 62.4% precisó intervención nutricional (100% suplementos orales, 21,4% cambios dietéticos, 5.2% nutrición parenteral). La intervención logró un aumento de ingesta real de 623 kcal y 27,3 g proteína/día, frenando la pérdida de peso y estabilizando las proteínas viscerales. La estancia fue 8,5 días mayor en nuestra muestra que en los pacientes que permanecieron normonutridos.

Conclusiones: uno de cada cinco ingresados normonutridos al ingreso desarrolló malnutrición en la hospitalización, asociando mayor estancia. La intervención nutricional puede mejorar la ingesta y el estado nutricional, por tanto, la vigilancia nutricional debería ser obligatoria.

Palabras clave:

Neoplasias hematológicas. Valoración nutricional. Estado nutricional. Malnutrición. Ingesta calórica.

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INTRODUCTION

Malnutrition is a common finding in cancer patients, which can affect disease progression and survival. Its appearance can be related to the malignancy itself or to treatment toxicity. Complications during cancer evolution, such as infections, may also increase the risk of malnutrition. A correlation between inflammation, oxidative stress parameters, and nutritional status in oncological diseases has been described in the literature. Particularly, hematological malignancies present abnormal blood cells that may have altered functions, facilitating an inflammatory medium. Therefore, in patients with leukemia undergoing chemotherapy, a high C-reactive protein/albumin ratio has been found, which may indicate a nutrition inflammatory risk (1).

Hospitalization represents an added risk factor for malnutrition development. Inpatients can present symptoms such as anorexia or nausea that reduce food consumption during admission. Additionally, aggressive cancer treatments are related to rejection of the hospital diet (2).

In large hospital series, the prevalence of malnutrition in hospitalized patients can reach 22.0%. However, in the elderly or in oncological inpatients, the frequency is even higher, particularly when admission is needed to provide a medical treatment or diagnostic workup (2). According to the results of the Spanish multicenter PREDyCEs study, 33.9% of the oncological patients were at nutritional risk at admission and 36.4% at discharge (3). Previous data collected in our own hospital revealed a prevalence of malnutrition in the Oncology and Hematology wards up to 47.7% (4). Even during their first admission to the Hematology Ward and before receiving any treatment for cancer, half of oncohematological inpatients had some degree of malnutrition or were at risk of suffering it (5).

Consequences of malnutrition in admitted cancer patients are severe. Patients with malnutrition have longer hospital stays, lower 90-day survival rates (2), increased hospitalization costs (6), and more hospital readmissions (4). In terms of mortality, undernutrition on admission is an independent predictor of early mortality in elderly cancer patients (7), and there is an upward trend between reduced intake and mortality in cancer patients (4). Moreover, inpatients exhibit worse results in terms of length of hospital stay and costs when they are admitted without malnutrition but develop it during their stay. This is particularly true with cancer, which is one of the conditions that show a significant association with a higher prevalence of malnutrition at discharge (3).

Therefore, screening of malnutrition and nutritional treatment is strongly justified, not only at admission but during all hospitalization. The systematic implementation of nutritional screening tools enables detection of patients at risk of malnutrition and taking appropriate action to reduce the negative impact of malnutrition in their prognosis and outcomes (8).

In order to continue the work in this field, we have designed a study to determine the incidence of new malnutrition in hematology inpatients and to assess the nutritional and clinical evolution of these patients after the Nutrition Unit intervention.

METHODS

During 2016, this prospective interventional cohort study was conducted in the Hematology Ward of the Complejo Asistencial Universitario de León (Spain). The Ethics and Clinical Research Committee of the hospital approved the study protocol, and patient anonymity was preserved.

The primary endpoint was to evaluate the incidence of malnutrition *de novo* during hospitalization in the Hematology Ward and the improvement in energy and protein intake after nutritional intervention. Our secondary endpoint was to observe if this newly diagnosed malnutrition was associated with an increase in length of hospital stay or mortality, in comparison with patients who did not developed malnutrition during hospitalization.

Inclusion criteria were patients older than 15 years admitted to the Hematology Ward from January 1st to December 31st, 2016. Exclusion criteria were pediatric patients, patients in their terminal phase, patients admitted for bone marrow transplant, and those with short hospitalizations (less than 24 hours).

During the first day of admission, a nutritional screening test was performed, and if negative, it was repeated weekly. The selected screening method was the Malnutrition Screening Tool (MST), validated in cancer patients and in patients during acute hospitalizations (9). It evaluates appetite and weight loss changes not requiring anthropometric measurements or biochemical parameters. A positive MST result (≥ 2 points) identifies individuals who are at risk of malnutrition. It is also a quick, simple, valid, and reliable tool that can be used by any health care worker. All screening tests were reviewed daily by the Clinical Nutrition and Dietetics Unit (CNDU). Patients with normal MST at admission but altered MST during their stay (positive MST result during weekly reevaluation) constituted our study population and were followed by the CNDU.

All recruited patients had a complete nutritional evaluation that included anthropometry, laboratory tests, and estimation of nutritional requirements. Following the Spanish Society of Enteral and Parenteral Nutrition (SENPE) and Spanish Society of Medical Documentation (SEDOM) definitions, we developed the nutritional classification (10). Patients were weighed standing on a Seca 762® mechanical scale with a precision of 0.1 kg wearing underwear and barefoot. Height was estimated using ulna length (11). Albumin, prealbumin, cholesterol, and protein bound to retinol (PBR) levels were measured with a blood test, following the usual practice of our laboratory. Energy requirements were calculated with the Harris-Benedict formula, using the actual weight for most patients, except in cases of obesity, when the adjusted weight was selected. A stress factor between 1.2 and 1.3 was added in most patients, following recommendations in hospitalized patients (12). In those patients with renal failure without renal replacement therapy, protein calculation was adjusted to severity of the disease (between 0.6 and 1 g of protein/kg weight/day) (13). During the first day of admission, we assessed the 24-hour intake through a semiquantitative self-administered test validated in our center. The 24-hour recall was divided into the four intakes of the hospital menu, and the amount ingested was registered using

the Nutrition Day scale (all, more than a half, half, less than half, nothing) (14,15). The intake was calculated based on the protein and energy content of the hospital diet components and the intake recorded by the patient during 24-hour recall.

Following standard clinical practice, in those patients who did not meet their energy or protein requirements, a nutritional treatment was prescribed (including changes in the type of diet, changes in the menu, prescription of oral supplements, enteral nutrition, and parenteral nutrition).

Finally, additional data regarding patients' evolution was collected, including length of hospital stay, three-month readmission rate, and in-hospital mortality. The results of the study group were compared to the results of the hematology inpatients that remained MST-negative throughout their admission.

The statistical analysis was performed with SPSS 21.0 (SPSS Inc., Chicago, IL, USA). The normal distribution of quantitative variables was examined using the Kolmogorov-Smirnov test. Variables matching normal distribution were presented as mean and standard deviation (SD) and those without normal distribution, as median and interquartile range (IQR). Quantitative variables were compared using Mann-Whitney, Student's t, and Wilcoxon tests for independent or related samples, respectively. Categorical variables were expressed as percentages and compared using the Chi-square test. A p value lower than 0.05 was considered as statistically significant.

RESULTS

Throughout the study period, 336 patients were admitted to the Hematology Ward. However, after applying exclusion criteria, nutritional screening with the MST was indicated and performed in 276 patients. Figure 1 shows the flowchart of the patients.

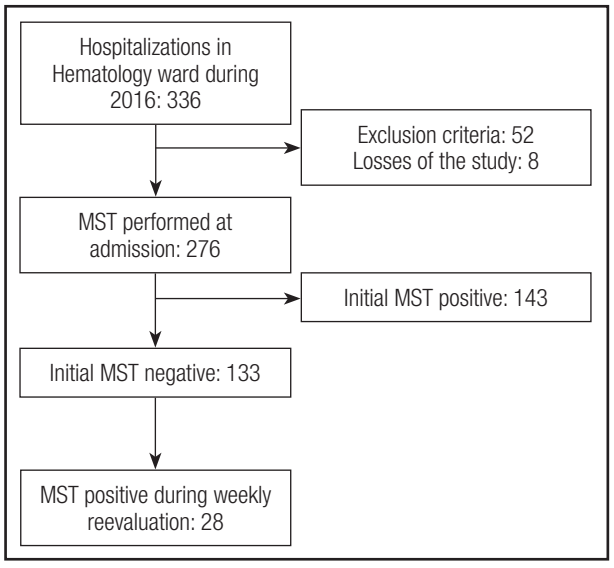

Figura 1.

Flow-chart of study patients.

DEMOGRAPHICS AND NUTRITIONAL ASSESSMENT

Baseline characteristics and the results of the complete nutritional evaluation of the patients are shown in table I.

The 28 patients included were hospitalized for a median of 22.5 (IQR 7-100) days, and the MST became positive on day 14.7 (SD 8.6) of hospitalization.

INCIDENCE OF NEWLY DIAGNOSED MALNUTRITION

Twenty-eight of the 133 patients with normal nutritional screening at admission developed malnutrition during hospitalization. This represented a 21% rate of newly diagnosed malnutrition in 2016 (incidence: 2.1 per 1,000 patients/year).

NUTRITIONAL INTERVENTION

A nutritional intervention was necessary in 64.2% of the patients with newly diagnosed malnutrition. All of these patients

Table I. Baseline characteristics of the patients

Age (years) (mean and SD)	63.4 (18.5)
Sex (% males)	60.7%
Diagnoses: n (%)	
Hematological malignancies	20 (71.4%)
Autoimmune diseases	6 (21.4%)
Myelodysplastic syndromes	1 (3.6%)
Other diagnoses	1 (3.6%)
Cause of admission: n (%)	
Cancer staging and/or therapy	12 (42.8%)
Infectious complications	4 (14.2%)
Hematological complications	7 (25%)
Other causes	5 (17.8%)
Nutritional status (%)	
Well-nourished	0
Energy malnutrition:	
Mild	3 (10.7%)
Moderate	1 (3.5%)
Severe	3 (10.7%)
Protein-energy malnutrition:	
Mild	0
Moderate	7 (25%)
Severe	7 (25%)
Protein malnutrition	5 (17.8%)
Not available	2 (7.1%)
Nutritional requirements calculated (mean and SD)	
Caloric (kcal)	1,610 (425.1)
Protein (g)	81.1 (20.1)

needed artificial support with oral supplements at any time, and some required more than one intervention. Therefore, a change in the type of diet was also needed in 21.4% of patients, and parenteral nutrition was indicated in two patients. No prescriptions of nutritional support by enteral access were registered in our population.

Figure 2 describes the energy and protein intake of the patients before and after the intervention. We observed that before the intervention, patients consumed a mean of 145 kcal and 17.8 g of protein below their theoretical requirements. However, after nutritional support, the real intake significantly increased to 623 kcal and 27.3 g of protein per day.

Regarding nutritional evolution, our intervention was able to slow the weight loss of patients. The median percentage of weight reduction before intervention was -4.5 (IQR -12.1 to 4.22), while after initiating nutritional support, it was -0.5 (IQR -10.87 to 8.73), although differences did not reach statistical significance. Visceral protein stabilized after treatment, and even prealbumin and cholesterol experienced a tendency to slightly increase (not significant) (Fig. 3).

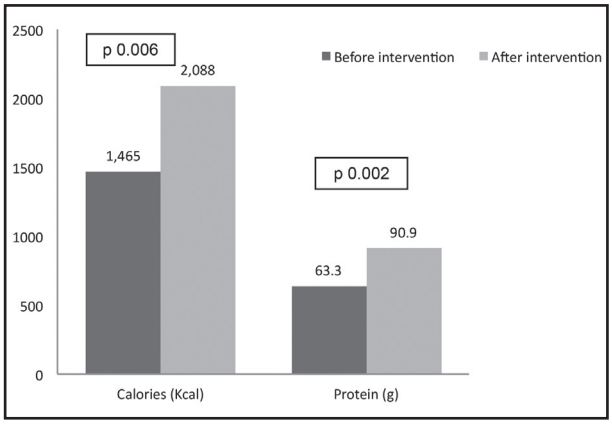

Figure 2.
Changes in nutritional intake after intervention.

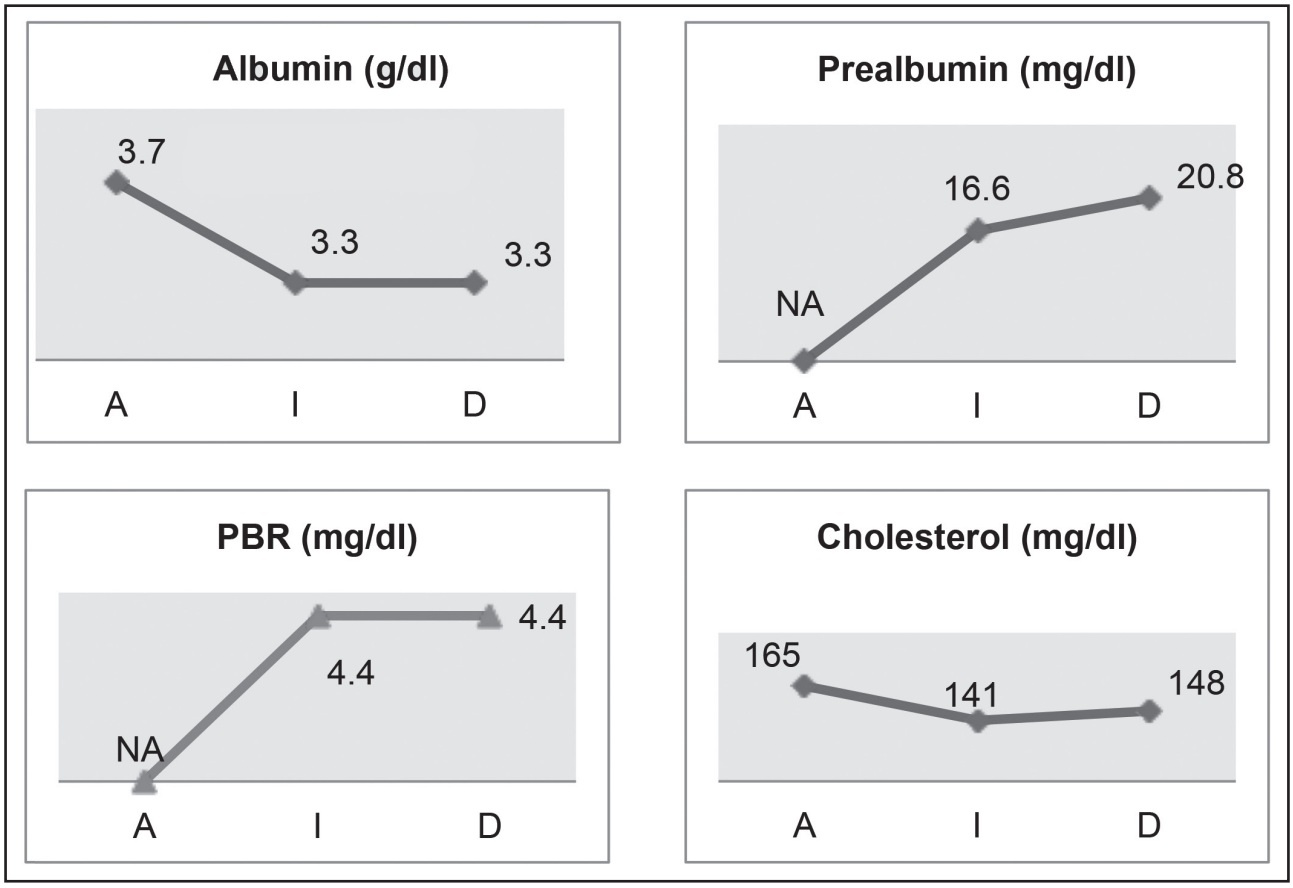

Figure 3.
Evolution of visceral protein parameters (NA: not available; A: on admission; I: at the moment of the intervention; D: at discharge).

EVOLUTION AND OUTCOMES OF MST-POSITIVE *VERSUS* MST-NEGATIVE PATIENTS

The results of the comparison between newly diagnosed malnourished patients and those who remained well-nourished during hospitalization are presented in table II.

Although both groups were comparable in terms of baseline characteristics, the development of malnutrition was associated with an 8.5-day longer length of stay, as table II shows.

DISCUSSION

This paper presents the results of systematic nutritional screening in hematological inpatients, which found that malnutrition appeared in one in five patients who were well-nourished at admission, prolonging their length of stay. A nutritional intervention in these patients improved or attenuated malnutrition in this setting.

Malnutrition is an important problem in hospitalized patients but is frequently undiagnosed. The literature indicates prevalence rates ranging from 20 to 50% (2), rising up to 30-70% in elderly patients (16). These wide ranges in malnutrition rates can be explained by the differences in the study populations (surgical or medical patients, elderly, etc.) and by the varied set of tools used to make the diagnosis. Some studies reported risk of malnutrition, detected by screening methods, while others reported malnutrition diagnosis after complete nutritional assessment.

Oncohematological inpatients are a population with a particular risk of malnutrition associated with the disease itself and its treatments. Several national and international studies have revealed that these patients exhibit a high prevalence of malnutrition at admission. One of the most relevant studies is the multicenter PREDyCES® study, performed in 1,707 inpatients, which found a 36.8% risk of malnutrition at admission in the oncohematological subgroup (3). In a recent study published by our group, we obtained a similar percentage of patients with positive screening (37.8%), and after complete nutritional assessment, 90.8% of our positive patients were found to be malnourished, being moderate or severe in 54.1% (17).

Hospitalization is a recognized risk factor of malnutrition as well. Metabolic stress, frequent fasting periods for diagnostic or therapeutic procedures, or deficiencies in hospital menus can deteriorate nutritional status throughout hospitalization. Therefore, a certain percentage of patients who are negative at the initial screening will presumably develop malnutrition during their stay. However, little is found in the literature about *de novo* malnutrition in this scenario. The PREDyCES study showed a decline tendency in the nutritional status during hospitalization that was more relevant in patients with hematological neoplasms (the prevalence of malnutrition rose from 36.8% at admission to 51.6% at discharge) (3). This represents a 14.8% increase in malnutrition during hospital stay, due to newly developed malnutrition. A cross-sectional study performed in hematology inpatients indicated a 41.3% prevalence of malnutrition risk at admission, 13.9% after a week, and 15.8% after two weeks of hospitalization (18). In our study, 143 of the 276 patients screened at admission were at risk of malnutrition (51.8%). However, 28 more patients developed malnutrition during their stay, representing an additional 10.1% increase in malnutrition during hospitalization (10.1% of all the patients screened and 21% of patients with negative screening at admission). Thus, in light of this data, we can expect a 10-15% increase in malnutrition after admission, justifying the need for periodical nutritional reevaluation.

After diagnosing malnutrition, the next step would be, logically, to perform a nutritional intervention. Nevertheless, nutritional support implementation is not yet included in routine clinical practice. A survey conducted on oncohematological patients revealed that half of them had not received any dietary advice, despite many being in the advanced stages of their disease (19). The PREDyCES study also revealed that 66.7% of the oncology inpatients at risk of malnutrition at discharge had not received any nutritional support during hospitalization (3). Therefore, despite its great frequency and medical relevance, the diagnosis of malnutrition is usually unnoticed, and treatment is not initiated until serious deterioration occurs (20). Raising awareness among medical personnel about the importance of malnutrition in the evolution of their patients would increase the recognition of malnutrition and achieve a more precocious implementation of nutritional support therapy.

Table II. Characteristics and outcomes in patients with positive and negative MST at weekly reevaluation

Variables	Positive MST at reevaluation n = 28	Negative MST at reevaluation n = 104	Statistical significance (p value)
Age (years) (mean and SD)	63.4 (18.5)	63.2 (16.4)	0.929
Sex (% males)	60.7%	60.5%	0.986
Diagnose of hematological malignancy (%)	71.4%	84.2%	0.170
Mortality during admission (%)	25%	26.3%	0.892
Length of stay (days) (median, IQR)	22.5 (35)	14 (16)	*< 0.01*
3-month readmission rate (%)	53.6%	65.8%	0.254

Nutritional intervention during hospitalization provides both health and cost benefits, reducing hospital costs and length of stay (21), even in patients with autologous hematopoietic stem cell transplantation (22). In our study, a nutritional intervention was necessary in two thirds of the patients with newly diagnosed malnutrition, and all of them needed at least oral supplements. This differs from the results of our previous study in malnourished patients at admission. Most of those patients only needed minor modifications in the menu or a change in the type of diet (40.3% and 16.5%, respectively), while oral supplements were prescribed only in 24.3% (18). The longer length of stay in patients with newly diagnosed malnutrition may explain the worse acceptance of the hospital diet and the higher need for supplements (22 days *vs* 15 days in malnourished patients at admission). Maintaining an adequate oral intake and good acceptance of the hospital diet during hospitalization can be challenging. During chemotherapy cycles, hematological inpatients present significant food rejection, especially with larger meals such as lunch and dinner, though light meals are better tolerated (23). Offering the patients certain foods such as fresh fruit, ice cream, or mashed potatoes may increase their appetite, morning being the best time of the day to consume them, and liquid textures having the greatest positive impact on food desires (24). Therefore, employing food options chosen by patients may be a strategy to improve dietary acceptance and might positively contribute to patients' well-being and nutrition. Another approach with good practical results was the implementation of trained food caregivers working in the Hematology Ward, which achieved an improvement in patients' energy intake (25).

Fulfillment of nutritional requirements is very difficult in hospitalized cancer patients, even when oral supplementation is prescribed. The efficacy of nutritional supplements may be limited by poor intake (26), especially if anorexia, gastrointestinal symptoms, or taste alteration are present. In the current study, before nutritional intervention, our patients consumed fewer calories and proteins than required, but after nutritional support, the real intake significantly increased, slowing down the weight loss and stabilizing the visceral proteins. This suggests that nutritional intervention had an effect on patients' nutritional evolution.

Despite these good results, the group of patients who developed *de novo* malnutrition presented worse evolution than patients who remained well-nourished during their hospital stay. Our data support the fact that the worse the nutritional status, the longer the length of stay (27). Thus, newly diagnosed malnutrition was associated with an 8.5-day longer hospitalization than that of well-nourished patients. In the PREDyCES study, patients at nutritional risk at discharge also showed a greater mean duration of hospitalization (12.1 days; 95% confidence interval [CI], 10.83-13.39) than well-nourished patients (8.6 days; 95% CI, 7.86-9.40) (3).

Other studies also related malnutrition with mortality and readmissions. In a study conducted in elderly patients, survival was lower in patients with a low calf circumference (< 31 cm), and malnutrition independently increased the risk of one-year death (7). Another study conducted in hospitalized patients showed that those "at risk" of malnutrition had a 3.7-fold higher risk of dying that patients "not at risk" (6). Fortunately, no significant differences in mortality and three-month readmission rate were found in our study.

LIMITATIONS AND STRENGTHS

The main limitations of our study were the lack of a control group, due to ethical reasons, and the short duration of the nutritional intervention (from when nutritional screening results were positive until hospital discharge). It was difficult to observe positive outcomes in a short period of time in cancer patients who were well-nourished upon admission and, after receiving aggressive treatments or experiencing complications during their stay, developed malnutrition.

As a strength, we have presented data about *de novo* malnutrition in hematology inpatients, which is little reported in literature. Our data strongly suggest that *de novo* malnutrition is frequent, it has consequences on patients' evolution (length of stay), and nutritional deterioration may be attenuated by nutritional support.

CONCLUSION

In conclusion, nutritional surveillance in well-nourished oncohematological inpatients must be mandatory because one in five patients can develop malnutrition during hospitalization. Malnutrition *de novo* is related with longer length of stay, but nutritional intervention may increase patients' protein and energy intake, stabilizing weight and decreasing protein malnutrition.

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