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Original article

Malnutrition associated with nutrition impact symptoms and localization of the disease: Results of a multicentric research on oncological nutrition

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SUMMARY

Background & aims: Malnutrition in cancer is an independent factor associated with negative clinical outcomes. The aim was to evaluate the prevalence and independent risk factors for malnutrition in hospitalized cancer patients using the Patient-Generated Subjective Global Assessment (PG-SGA).
Methods: We evaluated 4783 cancer patients, aged ≥20 years, in a hospital-based, multicenter, cross-sectional study. Patients were classified as well-nourished (PG-SGA Stage A), moderate/suspected malnutrition (PG-SGA Stage B), or severely malnourished (PG-SGA Stage C), and provided a score to define required nutritional interventions. Multivariate analysis was composed of the odds ratio (OR) estimated by ordinal polytomous logistic regression.
Results: 45.3% were classified as Stage B and 11.8% as Stage C. Moreover, 45.3% of the patients presented a need for nutritional intervention. The variables that presented the highest ORs for Stage B or Stage C were: problems with swallowing (OR 2.8, 95% confidence interval (CI) 2.2–3.4, $p < 0.001$), loss of appetite (OR 1.9, 95% CI 1.6–2.3, $p < 0.001$), vomiting (OR 1.8, 95% CI 1.5–2.3, $p < 0.001$), presence of more than 3 nutrition impact symptoms (OR 8.3, 95% CI 5.8–12, $p < 0.001$), and cancer site: lung (OR 4.6, 95% CI 3.2–6.6, $p < 0.001$), upper digestive cancer (OR 3.7, 95% CI 2.7–5.2, $p < 0.001$), and head and neck cancer (OR 3.7, 95% CI 2.7–5.2, $p < 0.001$). The score for Worksheet 4 on the PG-SGA had a higher association with malnutrition (OR 7.3, 95% CI 6.6–8.2, $p < 0.001$).
Conclusions: Malnutrition is highly prevalent in cancer patients in Brazil, and is associated with nutritional impact symptoms, cancer site and age ≥65 years.

1. Introduction

Malnutrition associated with cancer is a global public health problem, and is associated with a reduction in quality of life, tolerance to treatment, and therapeutic efficacy. Moreover, malnutrition increases risk of complications and hospital costs, constituting an important risk factor for the progression of disease and mortality [1,2]. Among the main factors involved in the development of malnutrition in cancer patients are reduced appetite, metabolic abnormalities, and symptoms related to cancer and antineoplastic treatment [3,4].

Patients with cancer are highly at risk for malnutrition [5]. Evaluation of the nutritional status of these patients at diagnosis and during treatment is of utmost importance, but is not a routine practice in health systems, although the American Society for

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Parenteral and Enteral Nutrition (ASPEN) recommends periodic nutritional assessment. In addition, objective nutritional assessment tools, traditionally used in clinics, can mask the diagnosis of malnutrition in cancer patients, who may have fluid excess and massive cancer masses [6]. In this context, the Patient-Generated Subjective Global Assessment (PG-SGA) is considered by the Oncology Nutrition Dietetic Practice Group of the Academy of Nutrition and Dietetics to be an adequate tool for the nutritional evaluation of cancer patients [7,8].

The PG-SGA is an adaptation of the Subjective Global Assessment (SGA) and has been validated to evaluate the nutritional status of cancer patients [9]. It is a non-invasive and complete instrument for assessing weight history, food intake, nutrition impact symptoms, activities and function, metabolic stress and body composition simultaneously, and has been used as a reference method for the nutritional evaluation of cancer patients in several studies [10–13].

The Scored PG-SGA is an easy to use nutrition assessment tool that allows quick identification and prioritization of malnutrition in hospitalized patients with cancer, and may optimize the use of resources designated to the health system by reducing hospitalization time and costs [1,2].

In Brazil, a multicenter study, the Brazilian Malnutrition Survey (IBRANUTRI), evaluated the prevalence of malnutrition in hospitalized patients with different diseases [14]; however, the prevalence of hospital malnutrition in cancer patients has not yet been examined in a multicenter and multiregional study.

Based on the above, the National Cancer Institute (INCA), a Brazilian governmental health institution, carried out a multicenter study, the Brazilian Survey of Oncology Nutrition (IBNO), with the objective of evaluating the prevalence and independent risk factors for malnutrition in hospitalized cancer patients in Brazil using the PG-SGA. IBNO is the largest nutritional status study conducted in Brazil among hospitalized cancer patients [15].

2. Patients and methods

2.1. Study design

IBNO is a hospital-based, multicenter, cross-sectional study of newly cancer patients admitted from August to November 2012, in 45 different public hospitals of Brazil [15].

2.2. Patients

The study population consisted of patients during hospital admission. Patients who met the following inclusion criteria were considered eligible: adults (age ≥20 years), with a confirmed diagnosis of cancer, and who agreed to participate in the study, signing the informed consent form. Patients admitted to intensive care units, in coma, mentally handicapped, and unable to independently respond to the PG-SGA questionnaire were not included in the study.

The project complied with ethical principles and was approved by the Research Ethics Committee of the National Cancer Institute Jose Alencar Gomes da Silva (INCA) under Registration No. 34746/2012.

2.3. Nutritional status and degree of malnutrition

The nutritional evaluation was performed using the PG-SGA [9], that was cross-culturally adapted and validated for use in the Brazilian Portuguese setting [16,17]. The PG-SGA was applied during the first 24 h of hospitalization by experienced clinical nutritionists. To guarantee data quality, the study methodology included the theoretical and practical training of all clinical nutritionists involved in the study in the 45 participating hospital units. This included the application of the PG-SGA and the completion of a form on a virtual platform, developed specifically for the collection of study data.

The PG-SGA includes two components. The first component was completed by the patient and includes four Boxes (1–4), addressing recent weight history (maximum score of 5), food intake (maximum score of 4), nutrition impact symptoms (maximum score of 24), and activities/function capacity (maximum score of 3). The second component was completed by a trained nutritionist and includes worksheets (1–4) that address: (1) weight loss percentage and score (2) disease and age, and its relation to nutritional requirements; (3) metabolic stress, including fever and use of corticoids (4) physical examination, including loss/deficit of subcutaneous fat, muscle, and presence of edema or ascites. Upon completion, the patient was classified as well nourished (Stage A), moderate or suspected malnutrition (Stage B), or severely malnourished (Stage C).

The PG-SGA provides a score to guide the nutritional intervention. A score between 0 and 1 indicates that no intervention is required at this time. Re-assessment on routine and regular basis during treatment, between 2 and 3 indicates patient & family education by dietitian, nurse, or other clinician with pharmacologic intervention as indicated by symptom survey and lab values as appropriate, between 4 and 8 indicates the need for intervention by dietitian, in conjunction with nurse or physician as indicated by symptoms, and ≥9 indicates a critical need for improved symptom management and/or nutrient intervention options (8). This final score is given from the sum of all Boxes and Worksheets [16–18].

2.4. Evaluation of risk factors for malnutrition

Information regarding cancer location, age, and sex were retrieved from the medical records. Cancer location was categorized by 9 groups according to prevalence and nutritional impact (Intestine [small intestine, colon, rectum, anus, anal canal]; upper digestive cancer [stomach, esophagus, pancreas and liver], breast, gynecological, head and neck, lung, lymphoma, leukemia, and other). Cancer locations with a low prevalence in the sample were grouped as “other”: prostate cancer (8.2%), thyroid, parathyroid, and parotid cancer (4.3%), cancer of the urinary system (3.7%), cancers of the skin (7%), cancer of bone and connective tissue (2.2%), other abdominal locations (1.3%), cancer of the penis and testes (1.2%), cancer of the central nervous system (1.1%), Hodgkin's disease (0.6%), and locations not specified in the medical record (2%).

2.5. Statistical analysis

The Kolmogorov–Smirnov test was used to test the sample distribution. Descriptive data analysis was performed using central tendency and dispersion measures. Mean and standard deviation (SD) were used for normally distributed variables and median and interquartile range (IQR) for not normally distributed numerical variables, and frequency (n) and percentage (%) for categorical data. The Bonferroni Post Hoc tests were performed to evaluate the sample size power to detect differences in the prevalence of malnutrition in hospitalized cancer patients from all five regions of Brazil using the PG-SGA.

The sample size (at least 134 patients per region) has a power of 80% to detect differences of prevalence of hospital malnutrition in cancer patients in the order of 38.7%–61.2% (major to minor prevalence of malnutrition). Moreover, with this sample size (at least 525 patients per region), the study has a power of 95% to detect differences of prevalence of hospital malnutrition in cancer

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patients in the order of 38.7%–47.4% (second minor difference observed) among large geographic regions, excepted by North Region (Table 1).

To evaluate the association between the socio-demographic variables, cancer/disease characteristics, and the PG-SGA results on the outcome variable, i.e., the three levels of nutritional status (Stage A, B, and C), the study employed ordinal polytomous regression using an odds ratio (OR) model [19] and the *Link Logit* function. The assumption of the proportional odds model was validated for most of the independent variables.

The multivariate analysis consisted of the odds ratio (OR) estimated by ordinal polytomous logistic regression in the presence of a subgroup of clinical variables, and nutrition impact symptoms in relation to the worst nutritional status (moderate/suspected malnutrition or severely malnourished), considering the interference of all variables simultaneously (gastrointestinal nutrition impact symptoms, and localization of the disease), evaluating the independent explanatory capacity.

Statistical analysis was performed using the SAS® System software, version 6.11 (SAS Institute Inc., Cary, North Carolina). The criterion for determining significance was $p < 0.05$.

3. Results

A total of 4783 cancer patients were included in the study, representing 13.5% of the 35,549 cancer patients admitted to Brazilian hospitals in the study period (Fig. 1).

Of the patients included in the study, 2504 (51.4%) were female. The mean age was 56.7 ± 14.6 years, with 1491 (31.2%) patients ≥ 65 years old (Table 2). According to the PG-SGA, 45.3% of the patients had moderate or suspected malnutrition or were severely malnourished (classified as Stage B (33.5%) or C (11.8%)). The median total PG-SGA score was 7 (IQR 3–15). When analyzed by categories, the median was 3 (IQR 1–6) in patients categorized as Stage A, 14 (IQR 9–19) as Stage B, and 20 (IQR 16–25) as Stage C. In total, 45.8% of the patients had a total score ≥9, indicating a critical need for nutritional intervention and/or symptom management.

The variables presented in Table 3 were identified in the univariate analysis as a significant risk factor for malnutrition.

In the multivariate analysis, it was observed that with regard to cancer location, lung cancer had a stronger association with malnutrition (OR 4.59, 95% confidence interval (CI) 3.18–6.63, $p < 0.001$), followed by upper digestive cancer (OR 4.51, 95% CI 3.31–6.1, $p < 0.001$), and head and neck cancer (OR 3.70, 95% CI 2.66–5.15, $p < 0.001$) (Table 4).

Patients with more than 3 symptoms were at a greater risk of moderate or suspected malnutrition or severe malnutrition, with an OR of 8.34 (95% CI 5.8–12, $p < 0.001$). The presence of more than 3 nutrition impact symptoms was found in 34% of the patients with moderate or suspected malnutrition (Stage B) and in 51.8% of the severely malnourished patients (Stage C) (see Table 4).

The symptom that presented the strongest association with malnutrition was difficulty swallowing (OR 2.75, 95% CI 2.22–3.41, $p < 0.001$), followed by anorexia (OR 1.93, 95% CI 1.64–2.28, $p < 0.001$), vomiting (OR 1.84, 95% CI 1.48–2.29, $p < 0.001$), feeling full quickly (OR 1.40, 95% CI 1.16–1.69, $p < 0.001$), diarrhea (OR 1.33, 95% CI 1.01–1.76, $p = 0.045$), and nausea (OR 1.28, 95% CI 1.06–1.54, $p = 0.008$).

4. Discussion

This is the largest multicenter study in Brazil that assessed the nutritional status of Brazilian patients with cancer. In this study, the prevalence and independent risk factors for malnutrition were evaluated in 4783 cancer patients that were hospitalized in 45 public and private hospitals in the five regions of Brazil, using the PG-SGA. Almost half of the patients (45.3%) had moderate/suspected malnutrition or severe malnutrition (Stage B + C), and 45.8% of the patients presented a critical need for nutritional intervention and/or symptom management (PG-SGA score ≥9). The factors that presented the highest OR for malnutrition were: problems swallowing; loss of appetite and vomiting; the presence of more than 3 nutrition impact symptoms; cancer site, i.e. lung, upper digestive or head and neck cancer; and age ≥65 years.

The etiology of malnutrition in cancer patients is complex and multifactorial, and may be influenced by the location and type of tumor, stage of the disease, side effects of the treatment, socioeconomic status, functional performance, nutrition impact symptoms, and inadequate nutritional therapy [22,23]. The secondary effects of these treatments in relation to nutritional alterations are well documented [20] and the high prevalence of malnutrition found in this study is quite similar to that reported in the literature. In a Spanish study in 781 patients with advanced cancer, the prevalence of moderate/suspected malnutrition and severe malnutrition was found to be 52%, also using the PG-SGA [20]. In a Brazilian study in 4000 patients that were hospitalized for various diseases, the prevalence of malnutrition was 66.3% among patients hospitalized for cancer, according to the SGA [13]. In contrast, in a multicenter study of 2248 cancer patients hospitalized in China, the prevalence of malnutrition was only 19.7–26.8% using the NRS 2002 [21]. The high prevalence of hospital malnutrition found in this study may be a result of the regional, social, and economic heterogeneity associated with the lack of awareness among health teams concerning the importance of routine nutritional status assessment. Indeed, in previous Brazilian or Latin-American multicenter studies [14,22], it was observed that only 23.1% and 18.8% of medical records, respectively, had a record of the nutritional diagnosis of the patients.

The nutrition impact symptoms problems swallowing, loss of appetite and vomiting, and the presence of more than 3 nutrition impact symptoms were independent factors associated with malnutrition, and almost half of the patients (45.8%) required

Table 1
Analysis of the prevalence of malnutrition in the 5 regions of Brazil during November 2012.

Region	N = 35.549[a]	N = 4783[b] (13.5%)	A (54.7%)	B (33.5%)	C (11.8%)	B + C (45.3%)
South-East	17.397	1710 (9.8%)	50.9%	34.2%	14.9%	49.1%
South	8.144	700 (8.6%)	52.6%	36.7%	10.7%	47.4%
North-East	6.739	1.608 (23.9%)	61.3%	30.3%	8.4%	38.7%
North	957	134 (14.0%)	38.8%	29.9%	31.3%	61.2%
Central-West	2.312	631 (27.3%)	54.4%	36.6%	9.0%	45.6%

PG-SGA classified the patients: well-be nourished, risk of malnutrition or moderately undernourished (B), and severely undernourished (C). Classified the patients with a risk of malnutrition, moderately undernourished or severely undernourished (B + C).

[a] Oncology population hospitalized in Brazil in November 2012.

[b] Oncology population admitted to the institutions that participated in the research in November 2012 and frequency of oncology population hospitalized in Brazil in November 2012.

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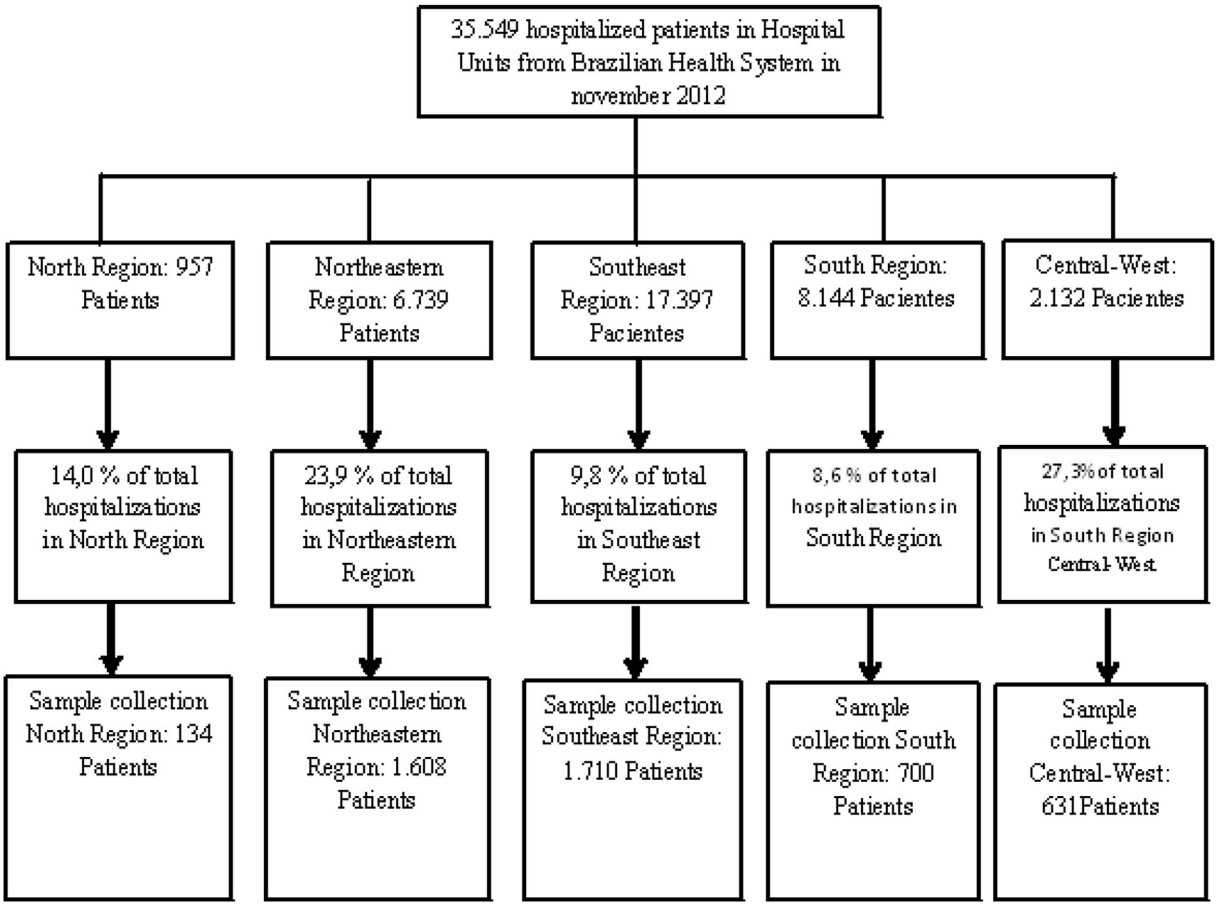

Fig. 1. Flowchart of sample collection.

critical nutritional intervention/symptom management. In previous studies conducted in Brazil [23], India [24], France [25], Canada [26], Spain [20], and Australia [1], it was observed that the symptoms that adversely affect food intake are similar to those found in our study. In this study, patients having problems swallowing presented a greater risk of malnutrition (OR 2.75, 95% CI 2.22–3.41), drawing attention to the immediate need for control of this symptom by multidisciplinary teams. In a study carried out in patients with advanced cancer, it was observed that dysphagia was the only symptom that was an independent predictor of survival, and it should be noted that malnutrition is considered an independent factor for the occurrence of death [26,27], which reinforces the need to prioritize management of the symptoms of nutritional impact due to their important contribution to mortality, reduction of quality of life, and increases in hospital costs [26–29].

Table 2
General characteristics of hospitalized cancer patients.

Variable	Total (n = 4783) n (%)
Gender	
Female	2504 (51.4)
Male	2279 (48.6)
Age (years)	
<65	3292 (68.8)
≥65	1491 (31.2)
Cancer site	
Intestine	760 (15.9)
Breast	674 (14.1)
Gynecological	580 (12.1)
Upper digestive cancer	375 (7.8)
Head and neck	353 (7.4)
Lung	193 (4.0)
Lymphoma	168 (3.5)
Leukemia	168 (3.5)
Other[a]	1512 (31.6)

[a] Corresponding to cancer with a low prevalence in the sample: 8.2% for prostate cancer, 4.3% for thyroid, parathyroid, and parotid cancer, 3.7% for cancer of the urinary system, 7% for cancer of the skin, 2.2% for cancer of bone and connective tissue, 1.3% for other abdominal locations, 1.2% for cancer of the penis and testes, 1.1% for cancer of the central nervous system, 0.6% for Hodgkin's disease, and 2% not specified in the medical record.

Lung cancer presented the highest OR for malnutrition (OR 4.59, 95% CI 3.18–6.63, $p < 0.001$), followed by cancer of the upper digestive cancer (OR 4.51, 95% CI 3.31–6.10, $p < 0.001$), and head and neck (OR 3.70, 95% CI 2.66–5.15, $p < 0.001$). These three cancer sites presented as an independent factor associated with malnutrition, as in the findings of Pressoir et al. [27], who found lower ORs than ours for upper digestive cancer (OR 3.39, 95% CI 1.89–6.10), and head and neck cancer (OR 2.28, 95% CI 1.53–3.41). Being aged ≥65 years was also an independent risk factor for malnutrition in this study, but previous studies in Brazil and Latin American also indicate an age >60 years as a risk factor for malnutrition in patients hospitalized for various reasons [14,22].

The tool used to evaluate the patients in the current study was the PG-SGA. The scored PG-SGA is used internationally as the reference method for proactive risk assessment (screening), assessment and monitoring nutritional status in patients with cancer., being one that has been most widely used in research and literature [18]. It is recommended by ASPEN [5] and has been adopted by the Brazilian National Consensus of Oncology Nutrition [18,30]. The PG-SGA is easy to apply, and takes an average time of few minutes to complete [18,20]. In our clinical practice, it takes 10–15 min to complete the questionnaire.

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Table 3
Univariate analysis of risk factors for malnutrition in hospitalized cancer patients, comparing well-nourished (A) with suspected/moderately (B) and severely undernourished (C).

Variable	Stage A (n = 2618) %	Stage B (n = 1601) %	Stage C (n = 564) %	OR (95% CI)
Gender				
Male	44.1	49.4	59.2	1.43 (1.28–1.59)*
Age				
≥65	25.6	37.7	38.5	1.70 (1.51–1.91)*
Cancer site				
Head and neck	4.9	8.7	15.2	5.94 (4.54–7.77)*
Upper digestive cancer	3.5	10.4	20.7	9.57 (7.37–12.4)*
Intestine	14.7	18.1	15.4	2.91 (2.33–3.62)*
Lung	2.1	5.8	8.2	7.28 (5.33–9.94)*
Gynecological	11.5	13.2	12.2	2.82 (2.23–3.56)*
Other	37.7	27.0	16.5	1.58 (1.29–1.93)*
Lymphoma	3.0	4.1	4.1	3.39 (2.42–4.74)*
Leukemia	3.4	4.0	2.5	2.49 (1.78–3.49)*
Breast	19.3	8.7	5.1	Reference
Nutrition impact symptoms				
None	66.6	17.4	4.3	Reference
1–3	27.6	48.6	44.0	8.62 (7.40–10.0)*
>3	5.8	34.0	51.8	27.3 (22.9–32.6)*
No appetite	11.3	47.5	56.6	6.28 (5.52–7.14)*
Nausea	8.4	30.5	42.7	4.74 (4.14–5.43)*
Vomiting	3.8	19.1	32.6	5.67 (4.84–6.66)*
Diarrhea	2.2	7.0	9.6	3.12 (2.46–3.95)*
Mouth sores	1.3	7.4	9.9	4.16 (3.31–5.23)*
Things taste funny or have no taste	6.1	23.3	27.1	3.75 (3.24–4.33)*
Smells bother me	6.6	24.1	28.7	3.77 (3.27–4.35)*
Problems swallowing	2.4	16.7	35.3	7.75 (6.54–9.19)*
Feel full quickly	6.0	23.9	32.4	4.41 (3.81–5.11)*
Dry mouth	10.3	29.9	40.4	3.81 (3.33–4.36)*

*$p < 0.05$; 95% CI = confidence interval; OR = odds ratio.

In conclusion, the prevalence of moderate and severe malnutrition is high in hospitalized cancer patients in Brazil and is associated with the occurrence of nutrition impact symptoms, cancer site, and being aged ≥65 years. The PG-SGA was successfully applied by nutritionists in the various participating centers, reiterating the importance of the participation of health professionals in the appropriate management of nutritional impact symptoms and in the completion of the professional component of the PG-SGA, to guarantee effective nutritional diagnosis of hospitalized cancer patients.

Table 4
Multivariate analysis of independent factors for malnutrition in hospitalized cancer patients, comparing well-nourished (A) with moderately and severely undernourished patients (B + C).

Variable	OR	95% CI
Gender		
Male	1.43*	1.23 to 1.67
Age		
≥65 years	1.83*	1.59 to 2.11
Cancer site		
Head and neck	3.70*	2.66 to 5.15
Upper digestive cancer	4.51*	3.31 to 6.1
Intestine	2.09*	1.61 to 2.72
Lung	4.59*	3.18 to 6.63
Gynecological	2.15*	1.65 to 2.80
Other	1.47*	1.15 to 1.89
Lymphoma	2.53*	1.69 to 3.78
Leukemia	2.17*	1.44 to 3.26
Breast	Reference	
Signs and symptoms		
None	Reference	
1–3	4.49*	4.0 to 6.0
>3	8.34*	5.8 to 12
Loss of appetite	1.93*	1.64 to 2.28
Nausea	1.28*	1.06 to 1.54
Vomiting	1.84*	1.48 to 2.29
Diarrhea	1.33*	1.01 to 1.76
Mouth sores	1.20	0.90 to 1.61
Things taste funny or have no taste	0.94	0.78 to 1.15
Smells bother me	0.89	0.72 to 1.09
Problems swallowing	2.75*	2.22 to 3.41
Feel full quickly	1.40*	1.16 to 1.69
Dry mouth	1.12	0.94 to 1.16

*$p < 0.05$; 95% CI = confidence interval; OR = odds ratio; adjusted for gender and age.

Author contribution

Pinho NB, Martucci RB, Rodrigues VD, D'Almeida CA designed research (project conception, development of overall research plan, and study oversight); Pinho NB, Martucci RB, Rodrigues VD, D'Almeida CA, Saunders C, Jager-Wittenaar H, Peres WAF conducted research and analyzed data and performed statistical analysis; Pinho NB, Martucci RB, Rodrigues VD, D'Almeida CA, Thuler LCS, Saunders C, Jager-Wittenaar H, Peres WAF wrote paper and had primary responsibility for final content.

Conflicts of interest

The authors declare no conflict of interest.

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