Nutritional status and primary tumour site in incurable cancer

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ABSTRACT

Objectives We aimed (1) to assess the nutritional status (NS) using different methods, according to the primary tumour site and (2) to evaluate the performance of these methods in patients with incurable cancer from a reference centre in Brazil.

Methods Cross-sectional analysis of data from patients admitted to the palliative care unit of a reference cancer centre in Brazil, between July 2016 and March 2020. The primary tumour site was the independent variable and the NS using different methods were the dependent variables. Logistic regressions were performed.

Results A total of 2,144 patients were included in the study. The most common primary tumour site was the upper gastrointestinal (GI) tract (18.0%), followed by gynaecological (17.6%) and head and neck (HN) (13.5%). Our results showed that patients with tumours of the upper GI tract followed by HN presented significantly higher risk of worse NS. *In contrast,* breast tumours, bone and connective tissues and melanoma presented inverse association. *The gynaecological cancer was variably associated with nutritional impairment, according to the assessment method.*

Conclusions *P*atients with incurable cancer present high prevalence of NS impairment, depending on the tumour site, shown to be elevated in patients with tumour in the upper GI tract.

Key messages

What was already known?
- Malnutrition commonly affects patients with incurable cancer.

What are the new findings?
- Patients with tumours site in the upper gastrointestinal tract and head and neck presented higher risk of worse nutritional status (NS).

What is their significance?
- (a) Clinical: patients with tumours with greater nutritional risk would need more frequent nutritional screening.
- (b) Research: pioneer study, analysis of the NS by different parameters and extensive cohort of patients in exclusive palliative care

INTRODUCTION

Malnutrition commonly affects patients with cancer and its magnitude varies according to the method of assessment, the primary tumour site, the extent of the disease and the concurrent treatment.[1–3] The reported prevalence ranges from about 20% to more than 70%, which is higher than those with other diseases, not only to the malignancy itself but also to the treatment involved.[4 5] It contributes to poor outcomes that include reduced physical functioning, decline in quality of life and, in some cases, more serious side effects, such as delirium related to thiamine deficiency.[6–10] In addition, increased mortality rates are also seen in individuals with impaired nutritional status (NS). Therefore, the identification of malnutrition is crucial for nutritional care plan regardless of the stage of the disease.

Different methods, such as anthropometric measurements, laboratory tests and subjective tools, can be used to assess the NS of individuals with cancer in different clinical contexts. There is no gold standard for determining a patient's NS. Each of these methods contains important methodological features (advantages and disadvantages) that can represent different nutritional domains, which explains part of the difference in the degree of the measured nutritional deviations.[2 3 11–14] Results of a multicentric research on oncological nutrition in Brazil demonstrated that patients with lung, gastrointestinal (GI) tract and head and neck (HN) cancer are at higher risk of malnutrition compared with other tumour sites.[13 15] Therefore, the nutritional impairment is more highly prevalent in advanced stages,

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although more than 50% of patients in the early stages have NS disorders.[1–3 5]

NS is irrevocably important for physical function and quality of life of patients with cancer. Since NS is a potentially modifiable factor, its monitoring must be early, continuous and individualised throughout the course of the oncological disease. In order to better guide this monitoring, the understanding of the relationship between the primary tumour site and the risk of malnutrition needs to be improved. Most studies that investigated the prevalence of nutritional impairment in patients with incurable cancer focused on a specific tumour site. Those who compare different tumour sites were not performed exclusively in the advanced stage of the disease. Thus, the aim of the present study was (1) to assess the NS using different methods of assessment and its association with the primary tumour site and (2) to evaluate the performance of these methods in patients with incurable cancer from a reference centre in Brazil, allowing the identification of the nutritional epidemiological profile of this group.

METHODS

Participants and data collection

This is an observational study carried out with patients with incurable cancer (metastatic or locally recurrent) referred to the palliative care unit (PCU) of the National Cancer Institute José Alencar Gomes da Silva (acromion: INCA) in Brazil. The study population has been described in more detail in previous publications.[2 3 8] The focus of care in the PCU is symptom oriented and the patients had distant metastasis (85.2%) or advanced locoregional tumour growth and were not receiving any antineoplastic treatment with curative intent.

Patients were evaluated during their first appointment at the PCU by trained researchers from July 2016 to March 2020. The eligibility criteria were patients with incurable cancer (locally recurrent or metastatic cancer proven by histological, cytological or radiological evidence, and who were not receiving any antineoplastic treatment with curative intent), both sexes, aged ≥20 years or older, Karnofsky Performance Status (KPS) ≥30% and ability to respond to the necessary information.

The following data were collected from the electronic medical records: primary tumor site and extent of the disease (stage, site of metastasis).

Primary tumour site

The primary tumour site was the independent variable and was categorized into 10 groups according to the prevalence found in the sample: upper GI tract (all, except colorectal cancer (CRC)), CRC, gynaecological, HN, breast, lung, bone and connective tissues (BCT), haematological, melanoma and 'others' (less prevalent tumour sites—central nervous system, kidney and urinary tract, male genital organs, peritoneum, mediastinum and unrecognised site).

NS assessment

Different tools and diagnostic classifications were used to assess NS.

Anthropometric measurements were obtained according to the methodology proposed by Lohman.[16] The body weight (kg) was measured using a Wiso Digital portable scale (W905, Brazil, 180 kg capacity). For hospitalized and bedridden patients, a bed-scale system (Stryker, Go Bed II, USA) was used. For height (m), an inextensible tape fixed to the wall was used. When the patient was unable to stand, height measurement was estimated by measuring knee height and calculated through the Chumlea *et al*[17] formulas. Body mass index (BMI; kg/m^2) was calculated as the body weight divided by the square of the height. Values of <20 kg/m^2 were recorded as low BMI. Percentage of weight loss (%WL) was calculated based on measured weight and patient-reported weight history in the past 6 months and values >5% were recorded as high %WL.[18]

Calf circumference (CC; cm) was measured with an inextensible tape by adopting the measurement of the largest perimeter and classified as low if ≤34 cm (male) and ≤33 cm (female).[19] Tricipital skinfold (TSF; mm) was measured at the midpoint between the acromion and the olecranon, in the dominant arm, using a Lange calliper. The values were divided into tertiles and values below the first tertiles were described as low TSF (≤6.3 mm (male) and ≤12.0 mm (female)). Arm circumference (AC; cm) was measured at the same point of TSF, using an inextensible measuring tape. Similarly, the lowest tertile was considered low AC (≤23.2 mm (male) and ≤23.0 mm (female)). Mid-upper arm muscle area (MUAMA; cm^2) was obtained through the equation proposed by Heymsfield *et al*,[20] using TSF and AC. Low MUAMA was characterised when the values were <32 cm^2 (male) and <18 cm^2 (female).[18]

BMI-adjusted WL-grade system (WLGS; 0–4) according to Martin *et al*[21] was used and patients were classified with nutritional impairment if the WLGS ≥3. Patient-Generated Subjective Global Assessment short form (PG-SGA SF), available at pt-global.org, was also used. This tool consists of a four-part questionnaire that includes questions about: (1) change in body weight: score from 0 to 5, (2) food intake: score from 0 to 4, (3) presence of nutritional impact symptoms: score from 0 to 24 and (4) performance status: scoring from 0 to 3. The total score of PG-SGA SF was the sum of the scores (0–36). Patients with values ≥9 were considered at nutritional risk.[22]

Cancer cachexia was classified according to the three diagnostic criteria: Wallengren *et al*[23] in two groups [non-cachectic (NCa) vs cachectic (Ca)] using

% WL+fatigue (intensity 0–10)+C reactive protein (CRP); Blum *et al*[24] in four groups (NCa vs precachectic (PCa) vs Ca vs refractory cachectic (RCa)) using combinations of changing body weight+BMI; Vigano *et al*[25] in four groups (NCa vs PCa vs Ca vs RCa) according to the combination of laboratory markers (CRP or leucocytes or albumin or haemoglobin) and/or %WL, and/or decreased food intake and/or low performance status (PG-SGA SF).

Statistical analysis

We processed statistical analysis using the Stata Data Analysis and Statistical Software (STATA) V.13.1. The Kolmogorov-Smirnov test was performed to assess distribution symmetry. Descriptive statistics (count/frequency (%), means±SD or median and IQR (percentile 25–75), as appropriate) were used to describe patient characteristics. The analysis of variance (ANOVA) test or the corresponding non-parametric Kruskall-Wallis (for continuous variables) and χ^2 test (for categorical variables) were used to compare differences according to the tumour site.

As primary tumour site was categorised into 10 groups, 10 *dummy* variables (D1–D10) were created and inserted one by one into each of our multiple regression equations. Thus, each tumour site was transformed into a corresponding binary categorical variable and could be compared with all other sites together (being considered the reference category).

The association between NS (dependent variables) and the primary tumour site (independent variable) was explored by performing 11 logistic multiple regressions for each dependent variable. In each of our models, we tested the OR and 95% CI of each tumour site (with all others as a reference) in relation to NS. For dependent variables that present more than two severity stages, such as cancer cachexia criteria (Blum *et al* and Vigano *et al*), ordinal logit models were conducted. All models were adjusted for age, KPS and current healthcare setting (inpatient vs outpatient). The values were considered statistically significant when p value <0.05.

RESULTS

A total of 2,144 patients were included in this study. The age predominantly was ≥60 years old (60.3%) and 58.6% were female. The most common primary tumour sites were upper GI tract (18.0%), followed by gynaecological (17.6%) and HN (13.5%). As shown in figure 1A, age<60 years were more frequent in gynaecological, breast and BCT sites (p<0.001) and male sex in upper GI tract, HN, lung, BCT, and other (p<0.001) sites.

Table 1 presents the relation between NS and the primary tumour site. As expect, the results showed that the prevalence of nutritional impairment in patients with incurable cancer is high regardless of the method used. Moreover, it was observed that patients with tumours located in the upper GI tract and HN presented worse NS when compared with patients with all the other cancer sites.

Patients with tumours in the upper GI tract (except for PG-SGA SF and Wallengren's cancer cachexia criteria), followed by HN (except for WLGS, PG-SGA SF, Blum, Vigano and Wallengren's cancer cachexia criteria) presented significantly higher risk of having worse NS. In contrast, primary tumour site in breasts show inverse association with nutritional impairment by low BMI, CC, AC, TSF and MUAMA, while tumour sites located in BCT and melanoma presented inverse association with four and three assessment methods, respectively. The gynaecological cancer was variably associated with nutritional impairment, according to the method of assessing (table 2).

DISCUSSION

This study presents the NS of patients with incurable cancer evaluated using different methods according to the primary tumour site at a referral cancer centre

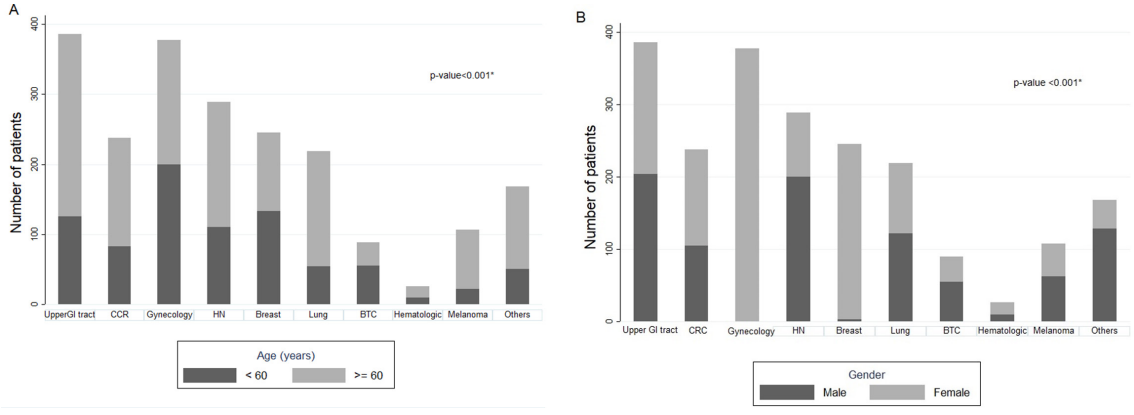

Figure 1 Demographic characteristics of patients with incurable cancer (n=2144) according to primary tumour site by age (A) and sex (B). BTC, bone and connective tissues ; CRC, colorectal cancer; GI, gastrointestinal; HN, head and neck. *P value refers to χ^2 for proportions.

Table 1 Clinical and nutritional characteristics of patients with incurable cancer according to the primary tumour site

Variables	n	Total	Upper GI tract n=387 (18.0%)	CRC* n=238 (11.1%)	Gynaecology† n=377 (17.6%)	HN‡ n=290 (13.5%)	Breast§ n=245 (11.4%)	Lung¶ n=219 (10.2%)	BCT** n=89 (4.2%)	Haematological†† n=26 (1.2%)	Melanoma‡‡ n=107 (5.0%)	Others§§ n=166 (7.8%)
KPS	2144	50 (40 to 60)	50 (40 to 50)‡	50 (40 to 60)‡§	50 (40 to 60)‡§	60 (50–70)§¶**††‡‡§§	40 (40–50)**††‡‡§§	50 (40–50)	50 (40–60)	50 (40–60)	50 (40–60)	50 (40–60)
BMI (kg/m^2)¶¶	1396	22.6 (5.4)	20.2 (4.2)*†‡§¶**††‡‡§§	23.2 (5.5)‡	24.1 (6.5)‡¶	21.0 (4.9)§**††‡‡§§	24.2 (5.0)¶	22.0 (5.1)††‡‡	24.2 (5.6)	25.4 (5.0)	24.5 (5.5)	23.6 (4.7)
WL in 6 months (%)***	1490	11.2 (4.4 to 20.0)	16.1 (6.4 to 5.4)*†‡§¶**††‡‡§§	10.6 (4.2 to 18.9)	12.6 (5.8 to 20.0)**††‡‡	11.8 (3.2–20.0)**††‡‡	10.4 (5.1–16.8)	11.7 (4.0–19.3)**††‡‡	7.2 (2.7–15.3)	7.6 (2.7–20.6)	7.7 (3.5–17.6)	10.3 (2.2–17.7)
CC (cm)¶¶												
Male	736	32.8 (6.9)	30.1 (4.3)**,§§	33.1 (4.4)	--	32.9 (23.1)	--	31.8 (7.5)	35.8 (5.9)	32.8 (3.0)	33.9 (4.3)	36.0 (3.0)
Female	946	32.9 (4.1)	31.0 (4.5)¶	32.0 (4.8)¶	32.4 (5.4)	32.6 (5.3)	33.2 (4.6)	37.0 (4.5)	33.0 (4.7)	35.0 (5.1)	34.2 (5.5)	33.3 (4.6)
AC (cm) ¶¶												
Male	870	24.9 (4.4)	22.7 (3.6)*‡¶**††‡‡§§	25.1 (4.3)**‡‡	--	24.1 (3.9)**‡‡	--	25.2 (4.0)**,‡‡	28.2 (5.8)††	25.1 (2.9)‡‡	27.4 (4.6)	26.3 (4.1)
Female	1200	26.0 (5.7)	23.8 (5.0)†‡§¶**††‡‡§§	25.4 (5.4)§,††,‡‡	25.7 (5.8)§,††,‡‡	26.6 (5.4)	27.5 (5.5)	26.2 (5.5)	27.0 (6.7)	27.8 (5.8)	27.7 (5.3)	26.2 (6.0)
TSF (mm)¶¶												
Male	840	9.9 (5.9)	7.2 (3.7)*,**,‡‡,§§	11.0 (6.6)‡,**	--	8.1 (4.3)¶,**,‡‡,§§	--	10.4 (6.0)**	14.0 (8.4)	9.3 (4.8)‡‡,§§	12.5 (6.0)	12.3 (5.5)
Female	1140	17.0 (8.8)	13.1 (7.5)*†‡§¶**††‡‡§§	16.4 (8.8)§	16.4 (8.4)§	17.2 (8.9)	20.6 (9.0)	17.1 (9.2)	17.9 (8.8)	18.7 (9.5)	19.0 (8.3)	17.4 (9.2)
MUAMA (cm^2)¶¶												
Male	846	28.7 (11.4)	24.9 (10.5)**‡‡	28.7 (10.8)**‡‡	--	27.3 (10.6)**‡‡	--	28.3 (9.8)**‡‡	35.5 (13.3)	30.7 (10.6)	35.4 (13.5)	31.4 (11.1)
Female	1134	27.6 (11.5)	24.7 (10.7)††‡‡	26.5 (10.7)††‡‡	27.2 (12.1)	28.8 (10.9)	28.3 (10.8)	29.0 (11.9)	29.2 (12.3)	32.2 (11.2)	33.5 (13.2)	27.6 (11.6)
WLGS†††	2145											
≥3		1638 (76.3)	316 (81.6)	181 (76.0)**††	293 (77.7)**††	225 (77.6)**††	180 (73.5)	166 (75.8)**††	59 (66.3)	18 (69.2)	77 (72.0)	123 (73.2)
PG-SGA SF (score)¶¶	2145	14.4 (6.8)	15.2 (6.5)‡‡‡§§	14.3 (6.9)†	16.0 (6.7)‡**‡‡§§	12.6 (6.8)§¶	14.8 (6.5)‡‡	14.7 (6.6)‡‡	13.2 (6.8)	14.7 (7.1)	12.0 (6.4)	12.7 (6.4)
Wallengren *et al*†††	1890											
Ca		191 (10.1)	33 (9.4)*‡‡	32 (15.0)‡§††‡‡§§	45 (14.0)§††‡‡§§	13 (4.9)¶**	19 (8.8)	22 (11.6)‡‡	9 (11.0)‡‡	2 (8.7)	4 (4.2)	12 (8.3)
Blum *et al*†††	1490											
Ca		817 (54.6)	149 (50.2)*,†,§,**,††,‡‡	99 (58.2)‡,§,§§	152 (61.5)‡,¶,§§	95 (45.0)§,¶,**,††,‡‡	102 (64.5)¶,§§	82 (53.2)	35 (59.3)	10 (58.8)	40 (58.8)	53 (46.5)
Rca		351 (23.5)	96 (32.3)*,†,§,¶,**,††,‡‡,§§	34 (20.0)‡,**,††,‡‡	51 (20.6)‡,**,††,‡‡	66 (31.3)§,¶,**,††,‡‡,§§	25 (15.8)¶,§§	35 (22.7)**,††,‡‡	8 (13.5)§§	2 (11.8)§§	7 (10.3)§§	27 (23.7)
Vigano *et al*†††	2070											

Continued

Table 1 Continued

Variables	n	Total	Upper GI tract n=387 (18.0%)	CRC* n=238 (11.1%)	Gynaecology† n=377 (17.6%)	HN‡ n=290 (13.5%)	Breast§ n=245 (11.4%)	Lung¶ n=219 (10.2%)	BCT** n=89 (4.2%)	Haematological†† n=26 (1.2%)	Melanoma‡‡ n=107 (5.0%)	Others§§ n=166 (7.8%)
Ca		260 (12.5)	54 (13.4)††	34 (14.6)††,§§	43 (11.7)††	46 (16.4)§,¶,††,§§	23 (9.8)††	22 (10.2)††	10 (12.0)††	1 (3.8)‡‡	14 (14.4)§§	13 (8.1)
Rca		886 (42.7)	191 (50.8)*,‡,¶,**,††,‡‡,§§	98 (42.1)‡,††,‡‡	176 (47.8)‡,**,††,‡‡,§§	96 (34.3)§,¶,‡‡	108 (46.1)**,††,‡‡,§§	91 (42.1)††,‡‡	32 (38.5)‡‡	9 (34.6)‡‡	24 (24.7)§§	61 (38.1)

Statistically significant difference (p<0.05) from:
*Lower GI tract.
†Gynaecological.
‡HN.
§Breast.
¶Lung.
**BTC.
††Melanoma.
‡‡Haematological.
§§Others.
¶¶Mean/SD/ANOVA.
***Median/IQR/Kruskal-Wallis test.
†††Number of observations/frequency/chi-square for proportions.
AC, arm circumference; ANOVA, analysis of variance; BCT, bone and connective tissues; BMI, body mass index; Ca, cachectic; CC, calf circumference; CRC, colorectal cancer; GI, gastrointestinal; HN, head and neck; KPS, Karnofsky Performance Status; MUAMA, mid-upper arm muscle area; n, number of observations; RCa, refractory cachectic; PG-SGA SF, Patient-Generated Subjective Global Assessment short form; TSF, tricipital skinfold; WL, weight loss; WLGS, WL grading system.

in Brazil, allowing to identify the nutritional epidemiological profile of this group. Our results showed that patients with incurable cancer present high prevalence of nutritional impairment but differ between the primary cancer sites. Patients with tumours of the upper GI tract, followed by HN, presented higher risk of a worse NS. *In contrast*, tumours located in breast, BCT and melanoma presented inverse association. The gynaecological cancer was variably associated with nutritional impairment, according to the assessment method.

In light of demographic, epidemiological and nutritional transitions, NS is irrevocably important for the health and quality of life of patients with incurable cancer.[8] However, ensuring its maintenance in a chronic, debilitating and care-dependent condition is a challenge. It should be noted that, despite of the fact that the impairment of NS is a characteristic present in most patients with cancer, it can still coexist with previous or concomitant excess body weight/obesity,[26] even in the advanced stage of the disease.

Since NS is a potentially modifiable factor, its monitoring must be early, continuous and individualized throughout the course of the oncological disease.[5] In clinical practice, the malnutrition in this group is underreported and, when it is recognised, it is not properly addressed. When we evaluate the data stratified according to tumour site subgroups, we find distinct prevalence of nutritional disorders. Thus, since there are barriers to an accurate nutritional assessment and management in clinical practice, it can be suggested that patients with primary tumour sites associated with greater nutritional risk would need more frequent nutritional screening to improve their NS, quality of life and care.[1 8 18 27]

Nutritional disorders in patients with cancer are known to differ from those of non-oncological etiology and are due to several changes caused by the tumor–host interaction, characterised by increased proinflammatory activity, catabolism, decreased protein reserves and food intake.[5] In addition, cancer refers to more than 100 different diseases, so NS disorders may also be different in relation to tumour types and vary according to the pathophysiology and genetic susceptibility underlying nutritional impairment.[28]

Of note, the high resting energy expenditure (REE) probably secondary to cancer, in part due to futile substrate cycles, is a recognised pathophysiologic alteration of the disease that contributes to the progression of WL and the burden of symptoms, accelerating the development of malnutrition.[29 30] A meta-analysis that compared the metabolically changes between cancer subjects and healthy controls showed an average increase in REE of 9.66 kJ per fat free mass kg/day in those with cancer.[28] *However, not all patients* with cancer are hypermetabolic.[31] In studies with patients from different primary tumour sites, those with elevated REE represented 26%[32] and 58%.[33]

Table 2 Nutritional status and its association with the primary tumour site in patients with incurable cancer

			Tumour location OR (95% CI)									
Models	Dependent variables	n	Upper GI tract	CRC	Gynaecology	HN	Breast	Lung	BCT	Haematological	Melanoma	Others
1*	BMI<20 kg/m^2	1396	**2.37 (1.79 to 3.15)**†	**0.64 (0.44 to 0.92)**‡	**0.63 (0.46 to 0.87)**‡	**2.69 (1.99 to 3.65)**†	**0.33 (0.21 to 0.52)**†	1.07 (0.74 to 1.56)	0.50 (0.25 to 1.01)	0.41 (0.11 to 1.50)	**0.46 (0.25–0.84)**‡	**0.61 (0.40–0.97)**‡
2*	WL>5% in 6 months	1490	**1.48 (1.08 to 2.03)**‡	0.90 (0.63 to 1.29)	1.36 (0.97 to 1.90)	1.08 (0.77 to 1.52)	0.98 (0.66 to 1.45)	0.73 (0.51 to 1.06)	0.66 (0.37 to 1.18)	0.62 (0.22 to 1.72)	0.74 (0.44–0.124)	0.68 (0.45–1.04)
3*	Low CC§	1683	**2.44 (1.76 to 3.40)**†	0.96 (0.69 to 1.35)	0.77 (0.58 to 1.02)	**1.90 (1.40 to 2.59)**†	**0.44 (0.31 to 0.61)**†	1.33 (0.93 to 1.91)	**0.51 (0.29 to 0.85)**†	0.46 (0.17 to 1.22)	**0.43 (0.28–0.68)**†	0.81 (0.55–1.19)
4*	Low AC¶	2070	**2.59 (2.05 to 3.26)**†	1.06 (0.79 to 1.42)	0.94 (0.73 to 1.19)	**1.61 (1.22 to 2.09)**‡	**0.46 (0.33 to 0.64)**†	0.73 (0.53 to 1.00)	**0.49 (0.29 to 0.83)**‡	0.51 (0.19 to 1.40)	**0.53 (0.32–0.86)**‡	**0.52 (0.35–0.75)**‡
5*	Low TS**	1980	**3.20 (2.52 to 4.03)**†	0.96 (0.71 to 1.30)	**0.46 (0.35 to 0.61)**†	**2.66 (2.03 to 3.49)**†	**0.16 (0.09 to 0.25)**†	0.97 (0.71 to 1.32)	0.76 (0.46 to 1.24)	0.73 (0.29 to 1.89)	0.62 (0.38–1.00)	**0.61 (0.41–0.87)**‡
6*	Low MUAMA††	1980	**2.39 (1.89 to 3.02)**†	1.14 (0.85 to 1.52)	**0.36 (0.28 to 0.47)**†	**2.70 (2.06 to 3.54)**†	**0.20 (0.13 to 0.29)**†	1.22 (0.90 to 1.64)	**0.61 (0.37 to 0.97)**‡	0.52 (0.20 to 1.32)	0.66 (0.42–1.04)	**1.46 (1.04–2.01)**‡
7*	WLGS>3	2145	**1.40 (1.06 to 1.87)**‡	1.01 (0.73 to 1.40)	1.10 (0.84 to 1.45)	1.23 (0.90 to 1.67)	0.80 (0.59 to 1.09)	0.89 (0.64 to 1.25)	**0.58 (0.37 to 0.93)**‡	0.65 (0.28 to 1.52)	0.83 (0.53–1.30)	0.83 (0.58–1.19)
8*	PG-SGA SF>9 pts	2145	1.25 (0.93 to 1.68)	1.13 (0.80 to 1.60)	**1.50 (1.09 to 2.06)**†	0.90 (0.67 to 1.21)	0.82 (0.58 to 1.17)	0.97 (0.68 to 1.39)	0.72 (0.42 to 1.23)	1.14 (0.41 to 3.15)	0.68 (0.43–1.06)	0.71 (0.48–1.03)
9*	Cachexia Wallengren	1890	0.98 (0.50 to 1.47)	**1.88 (1.23 to 2.86)**†	1.32 (0.91 to 1.92)	0.59 (0.32 to 1.06)	0.62 (0.37 to 1.05)	1.29 (0.80 to 2.10)	0.76 (0.36 to 1.60)	0.85 (0.19 to 3.72)	0.47 (0.17–1.31)	0.84 (0.45–1.58)
10‡‡	Caquexia Blum	1490	**1.66 (1.30 to 2.14)**‡	0.91 (0.67 to 1.23)	1.00 (0.77 to 1.30)	1.28 (0.95 to 1.71)	0.82 (0.60 to 1.13)	0.89 (0.65 to 1.23)	0.67 (0.41 to 1.09)	0.51 (0.21 to 1.28)	0.53 (0.33–1.84)	0.78 (0.54–1.14)
11‡‡	Cachexia Vigano	2070	**1.48 (1.19 to 1.83)**‡	1.11 (0.86 to 1.42)	1.22 (0.98 to 1.51)	0.93 (0.73 to 1.18)	0.89 (0.68 to 1.15)	0.91 (0.70 to 1.19)	0.74 (0.49 to 1.12)	0.57 (0.28 to 1.17)	0.53 (0.36–1.77)	0.75 (0.55–1.01)

In bold, data with statistically significant difference (p <0.05 or <0.001)

*Multivariate logistic regression.

†p<0.001.

‡p<0.05.

§Low CC: ≤34cm (male) and ≤33cm (female).

¶Low AC: <1st tertile (≤23.2mm (male) and ≤23.0mm (female)).

**Low TSF: <1st tertile (≤6.3mm (male) and ≤12.0mm (female)).

††Low MUAMA: <32cm^2 (male) and <18cm^2 (female).

‡‡Ordinal polytomous logistic regressions controlled by age, KPS, place of patient evaluation (outpatient vs hospitalisation).

§§

AC, arm circumference; BCT, bone and connective tissues; BMI, body mass index; CC, calf circumference; CRC, colorectar cancer; GI, gastrointestinal; HN, head and neck; KPS, Karnofsky Performance Status; MUAMA, mid-upper arm muscle area; PG-SGA SF, Patient-Generated Subjective Global Assessment short form; TSF, tricipital skinfold; WL, weight loss; WLGS, WL grading system.

Although many factors may be responsible for energy expenditure alteration in cancer, we can assume that the different tumour types may not affect the host's metabolism in the same way. One hypothesis is that elevations in REE are most remarkable in patients with tumours in metabolically demanding organs, such as those located in the upper GI tract, particularly in liver and pancreas,[30] which is in line with our findings. Thus, as the pathophysiology of cancer cachexia is driven by a combination of reduced food intake and abnormal metabolism, a different degree of nutritional risk related to different primary tumour sites is expected.[18]

We found that upper GI cancer presented the highest OR for nutritional impairment, which can be explained by tumour growth, bowel obstruction and other symptoms of nutritional impact such as anorexia, nausea, vomiting, diarrhea, esophagitis, mucositis and dysphagia.[34 35] A multicentric, cross-sectional study involving 4,783 patients with cancer, aged ≥20 years, found that among the factors that had a greater association with malnutrition, the symptoms of nutritional impact were highly prominent (dysphagia, hyporexia, emesis and the presence of more than 3 symptoms of nutritional impact).[13]

Pressoir *et al*,[36] evaluating data from 1,545 patients undergoing curative treatment or palliative care, reported that only patients with *upper GI tract* and HN tumours were independently associated with malnutrition assessed by low BMI or %WL in 6 months. *In the study of Sun et al*[37] *with 390 patients with advanced cancer, the highest prevalence of cancer cachexia was observed in pancreatic (89%), gastric (76.5%) and esophageal (52.9%) tumours, respectively. Another previous study showed that patients with upper GI cancers and HN had a higher OR for the diagnosis of moderate to severe malnutrition* (3.7, 95% CI 2.7 to 5.2 and 3.7, 95% CI 2.7 to 5.2, respectively).[13] Anker *et al*,[38] in a systematic review that gathered studies that added data from 31,047 individuals, estimated that 36.4% of the patients with cancer in the United States of America and 37.6% in the Europe had high risk of developing cancer cachexia. However, this risk ranged from 90% to 80% in those with primary tumour sites located in the liver, lung and pancreas to 30%–20% in those with thyroid, breast, melanoma and prostate cancer.

Breast, *BCT and melanoma cancer presented inverse association with nutritional impairment*. In breast cancer, for example, previous publications report a distinct nutritional pattern marked by excess weight and body fat. Garcia *et al*,[39] in a cross-sectional study conducted in a sample of 76 newly diagnosed breast cancer cases reported a high prevalence of overweight and obesity, with high body fat percentages and waist circumference values. Their average BMI was 27.3 (±5.5) kg/m^2. They also showed a high percentage of body fat, 38.3%, as well as a large waist circumference of 92.2 cm.

Gynaecological cancer was variably associated (directly-PG-SGA SF; and inversely associated-low BMI, TSF e MUAMA) with nutritional impairment according to the assessment method. *Patients with gynaecological tumours, assessed using the PG-SGA SF*, had a higher prevalence of nutritional risk when compared with the others. This tool can be considered a useful method to assess the NS of these patients in the contexts in which traditional anthropometric parameters may not be appropriate for nutritional assessment, because gynaecological cancer commonly presents pelvic mass or ascites, for example.[40] According to an observational, cross-sectional study in patients with cervical cancer, malnutrition assessed by *PG-SGA* was quite prevalent and this tool was significantly associated with the skeletal muscle index.[41] Another retrospective study, composed of 146 women with gynaecological tumours in different stages of treatment, found that 62.4% of them had nutritional risk or some level of malnutrition and the *PG-SGA* score median was 14 points.[42]

It is important to highlight the limitations of this work, among which the cross-sectional design deserves attention. The main variables analysed were obtained at the same time (baseline of the largest study), not allowing the assessment of temporality between their associations. However, our study is a pioneer in presenting an analysis of the NS by different diagnostic parameters in a large homogeneous cohort of patients with incurable cancer. There are several studies describing NS in patients with cancer, but we usually find it difficult to compare results due to methodological issues such as mixing patients at different stages of the disease or assessing NS by a single method, limiting the comparison of our results.

CONCLUSION

Patients with incurable cancer present high prevalence of NS impairment. However, the nutritional risk is different according to the primary tumour site, shown to be elevated in patients with the primary tumour site in upper GI tract.

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