Impairment of appetite and associated factors in older adults hospitalized with cancer

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Abstract

Objective: To investigate appetite impairment in older adults hospitalized with cancer and its association with nutritional status and cachexia. *Method*: A cross-sectional study, conducted with older adults men and women diagnosed with malignant neoplasia from July 2017 to March 2019 at a university hospital. The final sample consisted of 90 patients. Appetite was evaluated using the Cancer Appetite and Symptom Questionnaire (CASQ) and nutritional status was determined using the Patient-Generated Subjective Global Assessment (PG-SGA). Presence of cachexia was assessed by weight loss >5% in the last 6 months; or body mass index (BMI) <20 kg/m^2 and weight loss >2%; or appendicular skeletal muscle index consistent with sarcopenia and weight loss >2%. *Results*: There was a predominance of male (56.7%) self-declared non-white individuals (56.7%), with tumors in the gastrointestinal tract (75.6%) and median age of 67.0 years. 75.6% of the individuals have impaired appetite, 57.8% suspected malnutrition or malnutrition of some degree, 54.4% cachexia and 92.2% needed nutritional intervention. There was significant association between CASQ categories with nutritional status (p= 0.001) and presence of cachexia (p=0.050). After logistic regression analysis, malnutrition remained associated with impaired appetite assessed by CASQ score [OR: 4.68 (CI 95%: 1.50-14.56), p=0.008] *Conclusion*: The presence of malnutrition increased the chances of appetite impairment, which reinforces the need for early nutritional screening and intervention, in order to reduce and/or avoid nutritional problems.

Keywords: Health of the Elderly. Cancer. Nutritional Status. Cachexia. Appetite.

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INTRODUCTION

According to the World Health Organization (WHO), among non-communicable diseases and injuries, cancer has occupied second place in terms of causes of illness and death[1]. In older people, the incidence of new cases of cancer is higher than younger individuals, in addition to representing the greatest fatal victims of the disease, particularly those over 65 years of age, representing about 50% of cases and 70% of deaths by malignant neoplasms[2].

In this age group, the physiological changes characteristic of aging, such as changes in taste and lean mass reduction, are aggravated by cancer, and contribute to the emergence of malnutrition[3,4].

Malnutrition can be caused by insufficient energy supply, in addition to inadequate consumption and/or absorption of nutrients, which may or may not be related to inflammation[5]. However, when related to diseases such as cancer, it results mainly from systemic inflammation induced by the tumor, with consequent inappetence, significant loss of body weight and changes in body composition[6].

In 2015, the Lusa-Brazilian Survey of the Old-aged Oncology Nutrition (INCA)[7] pointed out that 33.2% of older people with cancer were malnourished and 39.8% were at nutritional risk. Previous studies have shown that the prevalence of these changes in older people with cancer ranges from 40% to 60%, associated with nutritional impact symptons (NIS), tumor staging and location, type of treatment and previous nutritional status[4,8].

Older people with cancer and malnutrition are even more vulnerable and are at greater risk of weight loss due to the disease's aggravations and associated comorbidities, increasing the risk of morbidity and mortality, length of stay, hospital readmissions, susceptibility to infections, reduced functionality and manifestation of cancer cachexia[9,10]. This, in turn, is another condition commonly observed in older people with cancer and coexisting with malnutrition, which makes the diagnosis and effective and appropriate treatment difficult[9].

Cancer cachexia is a type of malnutrition with chronic inflammation present and should not be identified as an advanced and final stage of malnutrition, however these diagnostic criteria are still a challenge for professionals and the scientific community[5].

Cachexia is recognized as a multifactorial syndrome characterized by involuntary weight loss, with continuous loss of skeletal muscle mass, with or without loss of fat mass, which cannot be fully reversed by conventional nutritional support that can lead to progressive functional impairment[11].

Both malnutrition and cachexia have overlapping clinical presentations and diagnostic criteria, however they differ widely in pathophysiology, etiology, prognosis and therapeutic approaches[11,5,9]. Malnutrition is specifically associated with the intake and use of nutrients and, therefore, a screening instrument that can also identify impairment in oral food intake becomes necessary[9].

Reduced food intake is a common condition in malnutrition and cancer cachexia. Even though they can occur at different times, both conditions potentiate progressive weight loss, worsen quality of life, response to treatment and postoperative complications[5,12].

People with cancer have a high prevalence of appetite disorders that can significantly impact their nutritional status and quality of life[13]. In older people with cancer, impaired appetite can be even more serious, as it adds to the anorexia of aging, a process characterized by age-related reduced appetite and food intake[14].

Given this scenario and the worsening nutritional status, commonly observed in older people with cancer, this study aimed to investigate the impairment of appetite in older people hospitalized with cancer and its association with nutritional status and the presence of cachexia.

METHOD

This is a cross-sectional, non-probabilistic, convenience sampling study conducted at a tertiary public hospital in Vitória (ES), Brazil. Older people of both sexes, diagnosed with solid tumors (ICD: C00 to

C97), determined by the International Classification of Diseases for Oncology (ICD-O)[15] and who were admitted for surgical treatment in the Surgical and Reparatory and Internal Medicine Units, from July 2017 to May 2019 participated in the study.

Patients aged ≥60 years old[16], diagnosed with malignant neoplasm regardless of type and anatomical location, confirmed in medical records, evaluated in the first 48 hours of hospital admission, able to answer the applied instruments, with the possibility of having the anthropometric data measured directly and with the oral route preserved were included. Patients with cognitive and neurological alterations foreseen in the medical record, patients in respiratory isolation, in palliative care, who were using appetite-stimulating drugs, bedridden, in preoperative fasting and who did not present all the information investigated in the study were excluded. After this step, the final sample consisted of 90 older people with cancer.

Data collection took place through interviews by three researchers responsible for the study in the pre-surgical period, using specific protocols. In order to minimize possible sample selection and data collection biases, all researchers were properly trained to apply the instruments and to take anthropometric measurements. Hospitalizations and surgical indications were monitored daily so that all older people during the study period could be considered.

Appetite impairment was the dependent variable assessed. The independent variables investigated were: sociodemographic (age, sex, self-reported race/color), clinical (tumor location) and anthropometric [body mass (kg), height (m)]. As for race/color, this was grouped into whites and non-whites, for those who declared themselves yellow, brown and black[17]. Tumor location was obtained from medical records and grouped into two categories: gastrointestinal tract (GIT) - esophagus, stomach, duodenum, colon, rectum, appendix and adnexal glands (pancreas, liver and biliary tract); non-GIT: lung, blood, head and neck, prostate, skin, mediastinum, ovary, chest and pelvis.

For the present study, body mass (kg) and height (m) were directly measured, according to the technique recommended by the WHO[18]. Body mass was measured with the aid of a Tanita® tetrapolar bioimpedance scale, with a maximum capacity of 100kg and precision of 100g. To measure height, the AlturExata® portable stadiometer was used, with a bilateral scale in millimeters and a use capacity of 0.35 to 2.13 m. Body mass and height were used to calculate the body mass index (BMI). BMI was calculated by dividing current body mass (kg) by height squared (m).

The assessment of nutritional status was performed from the Patient-Generated Subjective Global Assessment (PG-SGA). The version translated and validated for Brazilian Portuguese by Gonzalez et al.[19], upon permission to use *PG-SGA/Pt-Global Platform* (www.pt-global.org). The PG-SGA is a subjective nutritional assessment and screening tool, indicated by the Brazilian Consensus on Oncology Nutrition[10] for the evaluation of cancer patients in Brazil.

The version used is divided into two parts. The first is answered by the patient and comprises questions related to nutritional risk symptoms common in cancer patients, such as functional deficit, weight changes, dietary changes and depression. The second part, completed by the researchers responsible for the study, assesses questions based on factors associated with the presence of metabolic stress (fever and use of corticosteroids), physical depletion (changes in fat reserves, muscle mass and water retention), percentage of weight loss in 1 month or 6 months and the presence of other factors related to the health condition such as cancer, pulmonary or cardiac cachexia, decubitus ulcer, presence of trauma, age over 65 years and acquired immunodeficiency syndrome (AIDS).

The PG-SGA allows classifying nutritional status into three categories: A= well nourished; B= Moderate/suspected malnutrition, C = Severely malnourished. This version also allows assessing the need for nutritional intervention, which is defined through a numerical score, where 0-1 points: no intervention required at this time. Re-assessment on routine and regular basis during treatment. 2-3 Patient & family education by dietitian, nurse, or other clinician with pharmacologic intervention as indicated by symptom survey and lab values as

appropriate. 4-8 Requires intervention by dietitian, in conjunction with nurse or physician as indicated by symptoms (Box 3). ≥ 9 Indicates a critical need for improved symptom management and/or nutrient intervention options.

Cachexia was identified according to the criteria defined by the International Consensus on Cachexia[11]: weight loss >5% in the last 6 months; or BMI<20 and any degree of weight loss >2%; or appendicular skeletal muscle index consistent with sarcopenia and any degree of weight loss >2%. In this study, all patients diagnosed with cachexia met the first criterion.

The dependent variable, appetite, was evaluated by the Cancer Appetite and Symptom Questionnaire (CASQ) from the translated and validated version for the Brazilian population with cancer[20]. The instrument assesses the presence of symptoms related to appetite, namely: presence of appetite; early satiety; lack of appetite; change in taste; pleasure in eating; presence of nausea; mood swings; changes in willingness to perform daily activities and presence of pain. The questions have answers arranged on a five-point Likert scale, with the exception of the question regarding pain, which presents answers ranging up to 6 points, being very mild or no pain, mild, moderate, severe, very severe. It is worth clarifying that four items of the instrument presented the response scale inverted in relation to the others. An equation proposed by Spexoto et al.[20] in order to generate a global score, which classifies the impairment of appetite into three categories: low (≤1 point); moderate (1–3 points) and severe (>3 points), for the present study, moderate and severe impairment were grouped.

A descriptive analysis expressed as median and percentiles was performed to describe continuous variables and absolute and relative frequency for categorical variables. The *Kolmogorov-Smirnov* test was used to verify the normality of quantitative variables. Only individuals with all data were included in the analysis, with no treatment for missing data.

To verify the association of proportions between nutritional status, the presence of cachexia and the need for nutritional intervention with the CASQ categories, Fisher's exact test or the chi-square test was used. For binary logistic regression, the PG-SGA categories B and C and the CASQ categories, moderate impairment and severe impairment, were grouped.

To determine the influence of the variables on appetite impairment identified by the CASQ (dependent variable) binary logistic regression analysis was used. The crude *Odds Ratio* (OR) was presented and after adjustments for sociodemographic variables. The adjustment variables were inserted in blocks: model 1: age and sex and model 2: age, sex and tumor location. The variables that presented $p \leq 0.05$ in the previous tests were included in the regression. The significance level adopted was $p \leq 0.05$ for all tests.

This study was approved by the Ethics and Research Committee of the Federal University of Espírito Santo, under number 2,141,932. All patients signed the Free Informed Consent Form (FICF), following resolutions 510/2016 and 466/12 of the National Health Council, which regulate research with human beings.

RESULTS

Table 1 shows the sociodemographic and clinical characteristics of older people hospitalized with cancer. 90 older people participated in the study, with a median age of 67.0 years, minimum age of 60 years and maximum of 88 years.

The diagnosis of nutritional status, the need for nutritional intervention obtained by the PG-SGA, the presence of cachexia and the impairment of appetite, identified by the CASQ are shown in Table 2.

Table 3 shows the difference between the CASQ categories and nutritional status, presence of cachexia, need for nutritional intervention and tumor location. Malnourished older people were those with moderate and severe impairment of appetite (p=0.005), the same occurring for older people with cachexia (p=0.050).

Table 4 shows the results of the binary logistic regression models. Significant associations were found between impaired appetite, according to the

CASQ, and malnutrition, even after adjusting for age, sex and tumor location. Older people with suspected malnutrition or malnourished were 4.68 times more likely to have their appetite compromised when compared to well-nourished older people [OR: 4.68 (95% CI: 1.50–14.56) p=0.008].

Table 1. Demographic and clinical characteristics of older people hospitalized with cancer (n=90). Vitória (ES), 2019.

Age group (years)	n (%)
60–69.9	57 (63.3)
70–79.9	27 (30.0)
≥80	06 (6.7)
Sex	
Female	39 (43.3)
Male	51 (56.7)
Race/color	
White	39 (43.3)
Non-white	51 (56.7)
Tumor location	
Gastrointestinal tract (GIT)	68 (75.6)
Non-GIT	22 (24.4)

Table 2. Nutritional status, need for nutritional intervention, presence of cachexia and impaired appetite in older people hospitalized with cancer (n=90). Vitória (ES), 2019.

Variables	Total n (%)
PG-SGA	
Well Nourished (A)	38 (42.2)
Moderate/suspected malnutrition (B)	48 (53.3)
Severely malnourished (C)	04 (4.5)
Presence of cachexia	
No cachexia	41 (45.6)
With cachexia	49 (54.4)
Need for nutritional intervention	
0 - 1 point	01 (1.1)
2 - 3 points	06 (6.7)
4 - 8 points	22 (24.4)
≥ 9 points	61 (67.8)
Appetite impairment (CASQ)	
Low	22 (24.4)
Moderate	61 (67.8)
Severe	07 (7.8)

PG-SGA: Patient-Generated - Subjective Global Assessment; CASQ: Cancer Appetite and Symptoms Questionnaire.

Table 3. Nutritional status, presence of cachexia, need for nutritional intervention, and tumor location according to CASQ classifications in older people hospitalized with cancer (n=90). Vitória (ES), 2019.

Variables	Cancer Appetite and Symptons Questionnaire (CASQ)		
	Low	Moderate/Severe	*p* value
PG-SGA			0.005*
Well nourished	16 (42.1)	22 (57.9)	
Suspicious or moderately malnourished	6 (12.5)	42 (87.5)	
Severely malnourished	-	4 (100.0)	
Presence of cachexia			0.050**
No cachexia	14 (34.1)	27 (65.9)	
With cachexia	8 (16.3)	41 (83.7)	
Need for nutritional intervention			0.142*
0 - 1 point	-	1 (100.0)	
2 - 3 points	3 (50.0)	3 (50.0)	
4 - 8 points	8 (36.4)	14 (63.6)	
≥ 9 points	11 (18.0)	50 (82.0)	
Tumor Location			0.934**
Gastrointestinal tract (GIT)	16 (23.5)	52 (76.5)	
Non-GIT	6 (27.3)	16 (72.7)	

*Fisher's exact test; **Chi-square test; PG-SGA: Patient Generated Subjective Global Assessment.

Table 4. Association between the categories of appetite impairment, according to CASQ and nutritional status after crude and adjusted binary logistic regression analysis in older people hospitalized with cancer (n=90). Vitória (ES), 2019.

Variables	Crude OR (95%CI)	Model 1 OR (95%CI)	Model 2 OR (95%CI)
PG-SGA			
Well nourished	1	1	1
Suspected malnutrition / Malnourished	**5.57 (1.92 – 16.20)**	**4.66 (1.50 – 14.50)**	**4.68 (1.50 – 14.56)**
Presence of cachexia			
No cachexia	1	1	1
With cachexia	2.65 (0.98 – 7.19)	1.46 (0.47 – 4.51)	1.44 (0.46 – 4.50)

Model 1: adjusted for age and sex; Model 2: adjusted for age, sex and tumor location; Values in bold have $p<0.05$.

DISCUSSION

This study showed that malnutrition increased the chances of impaired appetite in older people hospitalized with cancer. An even higher proportion of malnutrition, cachexia, need for critical nutritional intervention and symptom control, and moderate to severe appetite impairment were observed.

Brazilian Enquiry on Oncology Nutrition (INCA)[21] evaluated, with the same instrument, cancer patients from 45 Brazilian institutions, and found that 55.6% of the population over 65 years of age was malnourished or at nutritional risk. Other studies that evaluated older people with cancer using the PG-SGA found a prevalence of malnutrition between 60.4% and 78.7%, showing the greater vulnerability

of this population[22,23]. This tool has been considered a prognostic and comprehensive factor in the identification of nutritional status in older people with cancer, as it more extensively assesses weight changes, nutritional impact symptoms (NIS) and the need for nutritional intervention[22,23].

Another risk factor for malnutrition may be related to the location of the cancer in the GIT[24], and which was in greater proportion in this study. Tumors located in the GIT directly impact the process of ingestion, digestion and absorption of nutrients, such as the presence of obstructive tumors, dysphagia, odynophagia and vomiting, often associated with cancer, which will compromise food intake and, consequently, the nutritional status[24,25].

A cross-sectional study carried out in Brazil that evaluated patients with cancer in the GIT treated surgically showed that 63% of patients with tumors located in the upper GIT showed changes in appetite and 60% had compromised food intake[26]. For those with tumors in the lower GIT, the prevalences were 45% and 36%, respectively.[26]. Also in this study, it was observed that 46.3% of the patients were severely malnourished and 29.3% were suspected of being malnourished or moderately malnourished[26].

The high prevalence of changes in appetite and food intake, and the prevalence of severe malnutrition in these patients, demonstrate the relevance of considering the location of the tumor on the nutritional status, especially when located in the GIT, so that clinical and nutritional managements are implemented early, in order to reduce and/or avoid these scenarios. Malnutrition can further compromise appetite in this population, which already has suppressed physiological responses, and potentiate the consequences of the disease and malnutrition itself.

Faced with an impaired nutritional status, the high need for critical nutritional intervention was another outcome observed in this study. A previous study carried out in the same hospital in 2016 showed that 91.4% of the patients evaluated had a need for critical nutritional intervention upon hospital admission, showing that this is a common condition in these patients[27].

Dos Santos et al.[28] when comparing the nutritional diagnosis obtained by the PG-SGA with objective anthropometric measures in older people undergoing anticancer treatment, they found that higher values of the PG-SGA score, which indicate the need for nutritional intervention, were associated with reduced food intake and lower anthropometric measurements related to body mass, muscle tissue and fat reserves. The PG-SGA score has been used in nutritional assessment because it has a high degree of reproducibility, sensitivity and specificity when compared to other validated methods[27].

The presence of cachexia was observed in more than half of the older people evaluated. Lima et al.[29] verified the frequency of cancer-related cachexia in patients with tumors in the GIT and found a prevalence of 56.3%. Specifically in older people with cancer, Dunne et al.[30] identified that 65.0% of the geriatric cancer population assessed in their study had cachexia. In this age group and with cancer, the risk of developing cachexia may be even higher, due to the changes inherent to aging that contribute to the worsening of the nutritional status, as discussed above[10], which reinforces the importance of considering it in the screening and initial nutritional assessment, especially in the hospital environment.

Another change that is also little considered in the evaluation of older people, especially with cancer, is the impairment of appetite, which was identified in most of the older people evaluated. Studies that evaluated the loss of appetite in individuals with cancer found that this condition is more frequent in older people and is more present with advancing age[31,32].

Decreased food intake is a symptom frequently observed in cancer patients, and is associated with several metabolic changes originated or resulting from the tumor[26]. These changes are mediated by several factors that modulate central nervous system receptors and neurons, especially cytokines, released by the immune system and the tumor[33]. These substances, such as IL-1, IL-6, TNF-α and IFNγ, can induce anorexia by antagonizing the action of Neuropeptide Y (NPY) in the hypothalamus, inducing the release of corticotropin releasing factor

(CRF), a potent anorectic factor and modulate significant changes in the α-subunits of the ventromedial nucleus (VMN) G protein, which participate in the control of food intake[33].

Antineoplastic therapies and related symptoms also interfere with the maintenance of appetite and nutritional status, as they can affect the perception of smell and taste and interfere with patients' ability to consume and digest food[26].

Thus, it is observed that the processes that lead to impaired appetite, malnutrition and cancer-related cachexia are integrated, and that generally result mainly from systemic inflammation and adverse effects of treatment.

In the studied sample, it was evidenced that patients with cancer cachexia had greater appetite impairment. When evaluating the presence of cachexia, loss of appetite and anorexia are factors that should be considered, and are associated with weight loss and exacerbation of this syndrome[11]. The CASQ is a predictor of weight loss, therefore, it can early identify the risk of developing cachexia[20].

Another significant association found was between impaired appetite and malnutrition, which was confirmed after binary logistic regression analysis. Reduced appetite and food intake are often associated with malnutrition, especially in patients with GIT cancer[34], however the causal relationship can only be defined in longitudinal studies.

De Pinho et al.[35] evaluated the relationship between PG-SGA-diagnosed malnutrition and NIS in cancer patients, and identified that swallowing problems, loss of appetite, vomiting, and the presence of more than three NIS were independent factors associated with malnutrition. The high frequency of NIS contributes to reduced food intake, worsening the patient's nutritional status[35].

Finally, it is necessary to reaffirm that malnutrition significantly compromises the physiological and metabolic responses of individuals, with even greater damage to older people with cancer, including appetite. Thus, our results point to the need for nutritional screening in order to prevent and/or reduce the impact of malnutrition in this population.

Although lack of appetite is one of the characteristics of cancer cachexia, this study found no association between the presence of cachexia and impaired appetite after adjusted logistic regression analysis. A possible explanation for this result may be the fact that a predominance of moderate appetite impairment was observed, which still does not characterize anorexia itself, a common condition in cachexia. It is believed that the observed impairment of appetite is more related to anorexia of aging than the presence of cachexia[14]. Another point to consider is that the diagnosis of cachexia in this study was defined by the percentage of weight loss over time and did not consider appetite as one of the criteria. Furthermore, anorexia is not a condition implicit in cachexia, especially in its onset. However, the design of this study does not allow us to assess this causality.

As a contribution, this study used a validated and specific tool to assess appetite in cancer patients that is easy to apply in clinical practice. It also demonstrates the relevance of appetite disorders and the presence of malnutrition and cachexia in older people with cancer, themes little explored in this population. The results also indicate the importance of diagnosing malnutrition and impaired appetite as a way to provide individualized nutritional counseling to manage the complications inherent in both situations. Multimodal clinical treatment is an indicated strategy that must be implemented and guaranteed in the care of older people with cancer.

Among the limitations of this study is its cross-sectional nature, which does not allow determining causal relationships, the absence of information on tumor staging and absence/presence of metastasis, since this is a reference hospital for surgical treatment and this information does not appear in the medical record. Another limitation refers to the fact that this study was carried out in a single public hospital with specific characteristics, which prevents the extrapolation of our results. However, the assessments and instruments were carefully applied by a small trained team.

CONCLUSION

Older people hospitalized with cancer had a high prevalence of malnutrition, cachexia, impaired appetite and the need for critical nutritional intervention. The presence of malnutrition increased the chances of appetite impairment in the studied population, which reinforces the need for early nutritional screening and intervention, especially in this population, in order to reduce and/or avoid nutritional problems.

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