

PREVALENCE OF CACHEXIA IN CANCER PATIENTS AND ASSOCIATED FACTORS

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Abstract: Introduction: Cancer cachexia is defined as a multifactorial syndrome characterized by a continuous loss of skeletal muscle mass. Chemotherapy is one of the anticancer therapy options, which can significantly influence the patient's food intake and nutritional status. **Goal:** to verify the prevalence of cachexia according to the consensus proposal in a sample of hospitalized cancer patients undergoing chemotherapy and the associated factors. **Methodology:** Cross-sectional, descriptive and analytical study carried out at the Hospital de Câncer de Pernambuco from January 2019 to April 2020. The sample consisted of patients admitted for chemotherapy treatment in the Clinical Oncology Ward of the hospital for chemotherapy treatment. Data were obtained through interviews, anthropometric assessment and collection of data recorded in medical records. Cachexia was evaluated by the criteria of the International Consensus on Cachexia. The variables associated with chemotherapy were: sociodemographic data, adverse effects of chemotherapy, nutritional status, nutritional risk and anorexia. **Results:** The sample consisted of 147 patients, adults (56.5%) and elderly (43.5%), half male (50.3%). The prevalence of cachexia was 39.5%, being associated with low weight ($p=0.003$), tumor location ($p=0.004$), being more common among patients with gastric (36.3%) and intestinal tumors (26.7%). There was also a strong association between cachexia and anorexia ($p<0.001$) and, to a lesser extent, symptoms such as nausea ($p=0.44$) and vomiting ($p=0.05$). **Conclusion:** Cachexia was high among patients. The association of factors such as tumor location, loss of appetite and gastrointestinal symptoms related to the disease and chemotherapy treatment proved to be favorable for the development of the syndrome. Additional follow-up studies are

needed so that cause and effect relationships can be carefully established.

Keywords: Cancer; chemotherapy; cachexia; prevalence; anorexia

INTRODUCTION

Cancer cachexia is defined as “a multifactorial syndrome characterized by an ongoing loss of skeletal muscle mass (with or without loss of fat mass) that cannot be fully reversed by conventional nutritional support and leads to progressive functional impairment. Cachexia is more common in patients with advanced cancer and tumors that affect the stomach, head and neck and in patients who already have malnutrition (FEARON; STRASSER et al., 2011).

Cachexia is a serious condition that affects more than 50% of all cancer patients and 80% of those with advanced cancer. The burden of cachexia is severe, accounting for 20% of cancer patient deaths. Cachectic individuals present worse quality of life, low tolerance to chemotherapy, radiotherapy and lower survival (ARGILES, 2005).

Typical symptoms of cachexia are weight loss, severe muscle wasting, anorexia, fatigue, high production of inflammatory cytokines. In cachexia, metabolic reprogramming occurs that favors energy waste, a catabolic state that leads to progressive weight loss with pronounced muscle loss (JOHNS; STEPHENS; FEARON, 2013).

Available evidence suggests that chemotherapy may play a key role in the development and maintenance of cachexia. Chemotherapy is often accompanied by numerous side effects, including nausea, diarrhea, anorexia. Some chemotherapeutics induce proteolysis, oxidative stress, inflammation and tissue injury, factors that contribute to the onset of cachexia (DAMRAUE et al, 2008).

Although cachexia is a common condition

and with serious repercussions for the oncology patient, diagnosis remains a challenge due to several confounding factors that make correct diagnosis difficult, and thus results in delay in Adequate treatment. Thus, the aim of this study was to assess the prevalence of cachexia in cancer patients hospitalized under chemotherapy treatment and to assess associated factors.

METHODOLOGY

Cross-sectional, descriptive and analytical study carried out at the Hospital de Câncer de Pernambuco (HCP), from January 2019 to April 2020. The sample consisted of patients admitted for chemotherapy treatment at the hospital's Clinical Oncology Infirmery during the period of the study. Data were obtained through interviews with the patient, anthropometric assessment and analysis of medical records. The sample calculation was performed considering a number of 1500 hospitalizations that occurred in the previous year in the period from January to December, a prevalence of 75.3% (DUVAL et al, 2015), a precision of 5% and a confidence interval than 95%, resulting in a minimum number of 120 patients to be studied. To correct eventual losses, this number was increased by 20%, making a total of 144 patients. Patients with a clinical diagnosis of cancer, admitted for chemotherapy and aged ≥ 18 years were included. Patients under 18 years of age, in the immediate postoperative period of surgery, who had ascites, anasarca, lower limb amputation, kidney disease on dialysis, pregnant women, hospitalized for treatments other than cancer, were excluded. The diagnostic criteria for cachexia used in this study correspond to the Brazilian Consensus on Cachexia/Anorexia in Palliative Care and the International Consensus for the Definition and Classification of Cachexia in Cancer, which considers weight loss equal to

or greater than 5% in the last six months or of 2% with a body mass index (BMI) $<20 \text{ kg/m}^2$, in addition to reduced food intake. (FEARON, 2011). Sociodemographic and clinical variables were evaluated (tumor location, staging – categorized into I, II, III and IV–, presence of comorbidities). The information was collected from the medical records of the Medical and Statistical Archive Service (SAME) and recorded in a specific form. The nutritional status of patients was assessed by collecting weight and height information. With the weight and height data, the body mass index (BMI) was calculated through the equation: $\text{BMI} = \text{weight}/\text{height}^2$. BMI was categorized as malnutrition for $\text{BMI} < 18.5 \text{ kg/m}^2$, eutrophy (≥ 18.5 to 25 kg/m^2) and Excess of weight (≥ 25 to 30 kg/m^2). Measurements of arm circumference, triceps skinfold thickness were also obtained. The evaluation of anorexia was performed using the simplified Nutritional Appetite Questionnaire (QNSA), an instrument recommended by the Cachexia and Sarcopenia Consensus. Chemotoxicity was assessed using a National Cancer Institute questionnaire encompassing some aspects of hematologic and non-hematologic toxicity. The questionnaire will be applied after the end of each cycle. The National Cancer Institute categorizes toxicity according to each questionnaire item in the following grades: 0 = no adverse event or within normal limits, 1 = mild adverse event, 2 = moderate adverse event, 3 = severe and undesirable adverse event, and 4 = life-threatening or disabling adverse event (NCI, 1999). This study was approved by the Research Ethics Committee involving human beings at the Hospital de Câncer de Pernambuco, under CAAE: 04347318.8.0000.5205.

RESULTS

The sample consisted of participants, half being male (50.3%), aged less than 60 years

(56.7%). The most frequently found tumors were gastric (36.3%), intestinal (26.7%), and head and neck (10.3%).

As for the nutritional assessment according to the BMI indicator, it was observed that most patients had eutrophy BMI (42.2%), followed by patients with malnutrition (31.3%). According to the BC, malnutrition was identified in 46.9% of the sample. Regarding nutritional risk, the prevalence was high, representing more than half of the sample (56.5%)

Regarding the presence of hematological chemotoxicity, most participants had anemia (71.4%), and a lower percentage of leukopenia (15.9%). Regarding gastrointestinal toxicity, the most prevalent symptoms were nausea (42.1%), vomiting (31.2%) and diarrhea (26.5%) respectively.

In the assessment of cachexia, using the concept according to the Brazilian Consensus on Cachexia/Anorexia in Palliative Care, 39.5% of the participants. presented the syndrome, and the entire sample presented fatigue (100%) and (48.3%) reported a reduction in food consumption due to anorexia. Furthermore, in relation to the body composition of the studied sample, there was greater depletion in adipose tissue, making up a total of 44.9% of the participants. As for muscle mass depletion, a lower percentage of 5.4% was obtained.

Cachexia was associated with factors involving the location of the tumor, with the gastrointestinal tract being the most prevalent ($p=0.004$); nutritional status of malnutrition ($p=0.003$) and anorexia (<0.001).

DISCUSSION

Cancer and nutritional status are directly related, so that physiological changes resulting from the disease can cause weight loss and malnutrition, which in turn, negatively influence the evolution of the

disease, response to treatment and survival time.

In the present study, half of the evaluated participants were male (50.3%), aged less than 60 years. Likewise, Rocha (2016) shows an average age similar to the study population, however, its largest sample was female (64.6%). Regarding the tumors found, the highest prevalence were those of the digestive tract, more specifically stomach and intestine. According to Lotici (2014), cancers in this region, by directly attacking the organs responsible for nutrition (intake, absorption and use of nutrients), are often associated with the incidence of cachexia.

The nutritional status evaluated through BMI showed an association with cachexia, however, as this parameter has limitations in relation to body composition, other tools such as CB, PCT and CMB were used to assess muscle and adipose reserve.

In the sample, there was a predominance of average weight loss of 10.58% in relation to the usual and current weight of the patients during the last months, with 68% with loss $\geq 5\%$, representing a large portion of the sample. This percentage was higher than that shown by Lociti (2014), who for the parameter % weight change, the General Group showed an average change of 4.5% and was classified as pre-cachexia at the initial moment, maintaining the percentage of change weight and classification at the end of treatment. Another study involving weight loss was developed by Silva (2017), who observed a significant association between males and the presence of weight loss, when compared to females (81.8% vs 54.1%; $p=0.027$); similarly, there was a significant association with the location of the tumor and the occurrence or number of weight loss. In individuals diagnosed with cancer of the digestive system, head and neck and male reproductive system, weight loss was

observed in 90%, 78.9% and 66.7% of the cases.

For symptoms preceding chemotherapy toxicity, it was found that most reported anorexia, nausea and vomiting. Similar results were found by Dúval (2015), who obtained a percentage of 55.8% of anorexia, 35.3% of nausea, 25.5% of vomiting, in addition to constipation 28.9%, with this No being evaluated in the present study. More than any other symptom, anorexia is seen as part of the first clinical and metabolic signs that precede cachexia, and can induce substantial and involuntary weight loss. This consists of loss of appetite, early satiety, a combination of both, or change in food preferences. These symptoms are not seen in all types of tumors, as stated by Silva (2006). Food intake may be compromised as a result of other symptoms: dysphagia, xerostomia, changes in taste and smell. Furthermore, it demonstrates that anorexia can be associated with obstruction of the gastrointestinal tract by solid tumors, with consequent complaints of dyspepsia, gastritis and stomatitis, dysphagia and odynophagia (DIAS, 2006).

The simplified Appetite Questionnaire (QNSA) was used to identify changes in the patients' appetite. More than half had a score equal to or ≤ 14 points, representing a risk of losing at least 5% of weight in six months for the sample. Because it is a simple and easy-to-apply questionnaire, its use may be relevant in clinical practice as a way of screening and providing nutritional assistance to hospitalized patients.

Another toxicity found was of hematological origin, with a high percentage for anemia, a complication observed after the end of each chemotherapy cycle. According to Ferreira et al. (2017), this is a frequent finding in cancer patients and has a negative impact on quality of life due to increased levels of fatigue. This condition can be

caused by the cancer process itself, the use of chemotherapy, or both.

The prevalence of cachexia was 39.5% in the total sample. In addition, a reduction in muscle mass was observed considering the AMC results. Concerning cachexia, it can induce systemic inflammation and cause metabolic changes, which, in combination with a decrease in body protein stores, can explain the poor prognosis in these patients (WEBSTER et al, 2020).

Regarding the factors associated with cachexia in cancer patients, it was observed that the symptoms are independent of the presence of the syndrome, since the cancer itself, with the activation of pro-inflammatory cytokines, and the chemotherapy treatment itself, contribute to such effects. However, this study could bring more speculations regarding the increase in toxicity in patients with the installed syndrome.

The assessment of nutritional status and early identification of cachexia is of fundamental importance for the elaboration of specific and individualized nutritional strategies for the patient's condition. Even though it is severe and common in cancer patients, cachexia is underdiagnosed and consequently inadequately treated, as it can also occur in non-malnourished individuals, that is, eutrophic and even overweight individuals. Therefore, in this study, grounded diagnostic criteria were used for better identification and clarification of conflicting factors about this syndrome.

CONCLUSION

Analyzing the results found, there was a high prevalence of cachexia among patients and an association of factors involving the location of the tumor, loss of appetite and gastrointestinal symptoms related to the disease and chemotherapy, proved to be favorable to the development of this

syndrome. Additional follow-up studies are needed so that cause and effect relationships can be carefully established.

Adequate nutritional screening, early intervention and constant monitoring of cancer patients before, during and after treatment must be incorporated into the routine of nutrition services so that adequate nutritional therapy can improve the clinical response and the patient's prognosis, preventing the onset reaches the state of cachexia.

REFERENCES

- ARGILES, J.M. et al. Molecular mechanisms involved in muscle wasting in cancer and ageing: cachexia versus sarcopenia. *The International Journal of Biochemistry & Cell Biology*, v.37, p. 1084–1104, 2005.
- Associação Brasileira de Cuidados Paliativos. Consenso Brasileiro De Caquexia e Anorexia em Cuidados Paliativos. *Rev Bras Cuidados Paliativos*. 2011;3(3 Supl 1):3-42.
- DAMRAUER JS, et al. Chemotherapy-induced muscle wasting: association with NF- κ B and cancer cachexia. *Basic and applied myology*. V.18:139–148, 2008.
- DIAS, M.V. et al. O grau de interferência dos sintomas gastrintestinais no estado nutricional do paciente com câncer em tratamento quimioterápico. *Revista Brasileira de Nutrição Clínica*, v.21,n.3, p. 211-8, 2006
- DUVAL, P.A. Prevalência de Caquexia Neoplásica e Fatores Associados na Internação Domiciliar. *Revista Brasileira de Cancerologia*, v.61, n.3, p.261-267, 2015.
- FEARON K ET AL. STRASSER F, ANKER SD, et al. Definition and classification of cancer cachexia: an international consensus. *Lancet Oncol*. 2011 May;12(5):489-95. doi: 10.1016/S1470-2045(10)70218-7. Epub 2011 Feb 4. PMID: 21296615.
- FERREIRA, REBECA GARCIA ROSA. FRANCO, LAURA FERREIRA DE REZENDE. Efeitos colaterais decorrentes do tratamento quimioterápico no câncer de mama: revisão bibliográfica. *Revista da Universidade Vale do Rio Verde*, v. 15, n. 2, p.633-638, 2017.
- JOHNS N, STEPHENS NA, FEARON KC. Muscle wasting in cancer. *The International Journal of Biochemistry & Cell Biology*, p.45: 2215–2229, 2013.
- NATIONAL CANCER INSTITUTE. Common Toxicity Criteria, Version 2.0. June 1, 1999.
- WEBSTER. J.M; KEMPEN L. J. A. P; HARDY R.S et al Inflammation and Skeletal Muscle Wasting During Cachexia. *Frontiers Physiology*, nov, v. 11, 597-675, 2020.

Parameters	Número (people)	Percentage (%)
Gender		
Male	74	50,3%
Female	73	49,7%
Age		
Adult	83	56,5%
Elderly	64	43,5%
Diabetes		
Yes	13	8,8%
No	134	21,2%
Hypertension		
Yes	50	34%
No	97	66%
Diagnosis		
Gastric cancer	53	36,3%
Bowel cancer	39	26,7%
Head and neck câncer	15	10,3%
Breast câncer	13	8,9%
Uterine/ovarian câncer	6	4,1%
Prostate câncer	5	3,4%
Lung câncer	5	3,4%
Others (liver, pancreas, skin, bone)	10	6,8%

Table 1- Demographic and clinical characteristics of cancer patients undergoing chemotherapy at a referral hospital in oncology, PE, 2019.

Parameters	Número (people)	Percentage (%)
IMC		
Malnutrition	46	31,3%
Eutrophy	62	42,2%
Excess of weight	39	26,5%
CB		
Malnutrition	66	46,9%
Eutrophy	62	42,2%
Excess of weight	16	10,9%
PCT		
Malnutrition	66	44,9%
Eutrophy	39	26,5%
Excess of weight	42	28,6%
CMB		
Depletion	61	41,5%
Adequate	86	58,5%
Nutritional risk		
With risk	83	56,5%
Without risk	64	43,5%

Table 2 – Nutritional characteristics of cancer patients undergoing chemotherapy treatment at a reference hospital in oncology, PE, 2019.

Parameters	Número (people)	Percentage (%)
Hemoglobin		
Anemia	105	71,4%
Normal	42	28,6%
Platelets		
Thrombocytopenia	11	7,6%
Adequate	134	92,4%
Leukocytes		
Leukopenia	23	15,9%
Adequate	87	60%
Leukocytosis	35	24,1%
Vomit		
0	101	68,7%
1	19	12,9%
2	25	17%
3	2	1,4%
4	-	-
Nausea		
0	85	57,8%
1	36	24,5%
2	26	17,7%
3	-	-
4	-	-
Estomatitis		
0	123	83,7%
1	18	12,2%
2	4,1	4,1%
3	-	-
4	-	-
Diarrhea		
0	108	73,5%
1	22	15%
2	12	8,2%
3	5	3,4%
4	-	-

Table 3 - Prevalence of chemotoxicity in cancer patients undergoing chemotherapy, at a referral hospital in oncology, PE, 2019.

Parameters	Number (people)	Percentage (%)
Cachexia		
Yes	58	39,5%
No	89	60,5%,
Anorexia		
Yes	71	48,3%
No	76	51,7%
Muscle depletion		
Yes	08	5,4%
No	139	94,6%
Adipose depletion		
Yes	66	44,9%
No	81	55,1%

Table 4 - Prevalence of cachexia and changes in diagnoses in cancer patients hospitalized under chemotherapy treatment at a referral hospital in oncology, PE, 2019.