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Association between weight loss and clinical-pathologic factors in oncological patients in chemotherapy treatment: a longitudinal study

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ABSTRACT. The present work aimed to study the relation between weight loss (WL) and clinical-pathologic factors in patients under chemotherapy treatment. It was a longitudinal observational study performed with patients assisted in an oncological ambulatory. The sample was composed of 402 patients, with an average age of 58.4 ± 13.6 years, of which 56.5% were women, and 51.7% were elderly. Regarding tumor localization, 12.9% were found in the head and neck, 22.6% in the breast, 10.2% in the lungs, 29.4% in the gastrointestinal tract (GI), and 24.9% in other body parts. A gradual fall of nutritional state in relation to BMI was observed, and the patients were advancing to malnutrition. When correlating the severe and non-severe weight loss (WL) with anthropometric data, a significant difference was obtained ($p < 0.05$). The overweight and obese patients had a greater severe WL in relation to the eutrophic and low weight group ($p < 0.05$). However, 67.3% of patients presented WL and a following nutritional state alteration, with the GI tract cancer presenting a significant difference, 37.4% ($p < 0.05$), in addition to severe WL ($p < 0.000$). Patients diagnosed with cancer, especially in the GI tract, and treated with chemotherapy, have higher chances of WL, which triggers a reduction of survival rate, with obesity and age being reliable predictors of a consequent severe WL.

Keywords: anthropometric; cancer; malnutrition; nutritional status.

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Introduction

Cancer has been reported as a tremendous public health problem, reaching 20 million of people worldwide, with an incidence of 600 thousand cases per year in Brazil (Instituto Nacional de Câncer [INCA], 2016). Although significant efforts were made in past decades, the current state of this disease is still unsatisfying (Luo, Sun, Sun & He, 2014).

Among all therapeutic options, chemotherapy is one of the most effective strategies to treat several types of tumors, especially the invasive and metastatic ones (Minko, Rodriguez-Rodriguez & Pozharov, 2013).

Therefore, the European Society for Clinical Nutrition and Metabolism (Cederholm et al., 2017) recently published criteria, based on a consensus, to malnutrition diagnosis. The diagnose aim to identify individuals with nutritional risk confirmed by BMI < 18.5 kg m^{-2} or WL in combination with BMI or low Fat-free mass index (FFMI) (Cederholm et al., 2015).

Opposing simple malnutrition, oncologic patients present a negative energy balance with skeletal muscle loss (Fearon et al., 2011). Malnutrition is expressed by WL with depletion of some body compartments or alteration in clinical, biochemical and nutritional parameters (Bozzetti, 2015). WL is considered severe when it represents 10% of habitual body weight (Mariani, Lo Vullo, Bozzetti, 2012).

Thus, WL is an indicator of malnutrition, which is strongly associated with negative results, mainly including increased mortality and decrease of health quality, in all stages and types of cancer (Bozzetti, 2015; Brewczyński, Jabłońska & Pawlicki, 2017). Due to tumor systemic effects and treatment side effects,

oncologic patients develop several levels of malnutrition (Van Bokhorst-De Van Der Schueren, 2005).

The treatment with chemotherapy is associated with an increased risk of toxicity, as well as a worse performance (Sun, Luo, Weiping, Sun & He, 2017); lower life quality and survival rate (Bozzetti, 2015; Caillet et al., 2017). In the study performed by Caillet et al. (2017), the patients presented a WL of 40 to 91.6% during chemotherapy treatment, depending on tumor localization.

Data regarding patients' weight loss and associated factors such as tumor localization and nutritional status are inexistent in the central-west region of Paraná state. Therefore, the objective of this study was to analyze the relation between nutritional status and WL and tumor localization of patients with cancer, who were receiving chemotherapy treatment in one of the oncological clinics situated in Guarapuava city.

Material and methods

A longitudinal observational study was performed from March 2016 to April 2017. This study was approved by the Ethics Committee of Research – COMEP/UNICENTRO, under process Nº. 1.371.989/2015.

The samples were composed of records of patients diagnosed with cancer registered in the Brazilian public health system (Sistema Único de Saúde – SUS), which were treated with chemotherapy and assisted in the oncologic ambulatory of a hospital in Guarapuava city, Paraná state. Patients' records without date and uncompleted or insufficient anthropometric data were excluded from the study.

The nutritional consultations registered in 402 patients' records were used in the present study. We analyzed the records of women and men of 20 to 87 years old, who were treated with chemotherapy between 2015 and April 2017. The collected data included age, gender, habitual weight (HW – the weight that the patients used to present), current weight (CW – assessed by professionals) and neoplasia localization.

The patients' nutritional status was determined by BMI expressed in kg m^{-2}, according to the adult category: < 18.5 kg m^{-2} low weight and/or malnutrition; 18.5 to 25.9 kg m^{-2} eutrophia; 25.0 to 29.9 kg m^{-2} overweight and ⩾ 30.0 kg m^{-2} obesity[12]. To elderlies: < 23 kg m^{-2}, low weight; 23 kg m^{-2} to 27,9 kg m^{-2} eutrophia; 28.0 kg m^{-2} to 29.9 kg m^{-2} overweight and ⩾ 30 kg m^{-2} obesity (Organização Pan-Americana de Saúde [OPAS], 2002).

The weight loss was calculated by the following formula: (HW-CW); and the WL percentage by: (HW-CW)/ HW x 100, which result was classified as: % < 0 = no weight loss, % = 0, stable; % ⩾ 0 < 5 = not severe weight loss; % ⩾ 5 < 10 = moderate weight loss and % ⩾ 10 = severe weight loss (Blackburn, Bistrian, Main, Schlamm & Smith, 1977).

Tumor localization was separated in groups: head and neck, gastrointestinal tract (GI tract), breast, lung, and others (Table 1).

Table 1. Groups classification and respective neoplastic localization.

Neoplastic group	Localization
Head and Neck	Mouth, larynx, pharynx, and thyroid.
GI tract	Esophagus, pancreas, stomach, colorectal and liver.
Breast	Breast.
Lung	Lung.
Others	Lymphoma, sarcoma, melanoma, cervix, ovary, testicle, penis, bladder, prostate e kidney.

Source: Elaborated by the authors

We analyzed the data by descriptive statistic, employing measures of central tendency, relative, and absolute frequency. The 'Kolmogorov Smirnov' test analyzed data distribution, and the correlation was done by 'Pearson' correlation coefficient. Mean of independent samples were compared using 'Student's' T-test. The comparison between the categorized data was performed using a chi-squared test.

Significance was accepted when p values were < 0.05, with a 95% confidence interval. Tabulation was performed using Microsoft Office Excel 2010®. The analyses were carried out using the statistic program Statistical Package for the Social Sciences® version 20.0 (IBM).

Results

From the 402 patients studied, 56.5% were women and 43.5% men. Regarding age, the average was 58.5 ± 13.6 years old, being 48.2% adults and 51.7% elderlies. The minimum age presented was 20 years old, and maximum age was 84. Regarding tumor localization, 29.4% of patients presented GI tract tumor, 22.6%

breast tumor, 12.9% head and neck tumor, 10.2% lung tumor, and 24.9% of the patients presented tumor in other body parts (Table 2).

Table 2. Sample characterization of patients with neoplasia during chemotherapy treatment, 2017.

Parameter	No. (%)	M (SD)
Gender		
Female	227 (56.5)	
Male	175 (43.5)	
Age (years old)		58.5 ± 13.6
Elderlies	208 (51.7)	
Adults	194 (48.2)	
Localization		
GI tract	118 (29.4)	
Others	100 (24.9)	
Breast	91 (22.6)	
Head and Neck	52 (12.9)	
Lung	41 (10.2)	

Note: M = Mean; SD = Standard Deviation; No. = number; % = Percentage. Source: Elaborated by the authors

Regarding general anthropometric characteristics of the sample, the average habitual weight and BMI were 71.9 ± 16.4 kg and 26.4 ± 5.3 kg m^{-2}, respectively. The average of current weight and BMI were 65.9 ± 15.9kg e 24.2 ± 5.3 kg m^{-2}, respectively. Disease duration had an average of 11.4 ± 11.4 months. The WL percentage was of 7.9 ± 11.6, and the weight loss presented in relation to habitual weight was 6.0 ± 8.8kg (Table 3).

Table 3. Anthropometric data and disease duration of patients with neoplasia during chemotherapy treatment, 2017.

Parameter	Mean ± SD	Min. – max,
Height (m)	1.6 ± 0.1	1.4 a 1.9
HW (kg)	71.9 ± 16.4	34 a 130
CW (kg)	65.9 ± 15.9	35 a 116
Habitual BMI (kg m^{-2})	26.4 ± 5.3	15.0 a 48.3
Current BMI (kg m^{-2})	24.2 ± 5.3	14.2 a 42.7
WL (kg)	6.0 ± 8.8	-27 a 55
% WL	7.9 ± 11.6	-38.6 a 47.8
Disease duration (months)	11.4 ± 11.4	0.2 a 120

Note: Results expressed in means and standard deviation, and minimum and maximum. HW= Habitual weight; CW = current weight; BMI = Body mass index; WL = weight loss; m = meters; kg = kilograms. Source: Elaborated by the authors

When the weight loss was correlated with current weight, an inverse correlation was observed ($p < 0.05$), in which, the higher the current weight, the lower the weight loss. The same significant inversely proportional correlation was found to current BMI ($p < 0.05$).

A positive correlation was found when the habitual weight and BMI were correlated with the weight loss, in which the higher the habitual weight or BMI, the higher patients' weight loss ($p < 0.05$). The height presented a positive relation with WL, in which the greater the height, the higher the WL ($p < 0.05$). In turn, the age and the disease duration did not demonstrate a significant correlation with weight loss in kg (Table 4).

Table 4. Correlation between weight loss (WL) and clinical and anthropometric data.

Parameter	R	p
Age (years old)	0.081	0.105
Current weight (kg)	-0.224	0.000**
Height (m)	0.109	0.029*
Current BMI (kg m^{-2})	-0.278	0.000**
Habitual weight (kg)	0.318	0.000**
Habitual BMI (kg m^{-2})	0.299	0.000**
%WL	0.964	0.000**
Disease duration (months)	0.023	0.645

Note: m = Meters; Kg (kilos); Pearson correlation test; *Significant difference at 5%; **Significant different at 1%. Source: Elaborated by the authors

When patients with and without severe WL were compared, the group with severe WL presented an average age of 59.7 ± 12.7 years old, and the other group demonstrated an average of 56.8 ± 14.5 years old,

which shows a significant difference ($p < 0.05$). Also, the current weight and BMI were compared with WL, and the group with severe weight loss demonstrated lower weight and BMI than the other group ($p < 0.05$). The group with severe weight loss presented greater means compared to the group without weight loss ($p < 0.05$). The height demonstrated no significant difference between groups (Table 5).

Table 5. Comparison between patients with severe and not severe weight loss regarding anthropometric parameters, age range, and disease duration, 2017.

Parameter	Severe WL (n = 227)	Not severe WL (n = 175)	p
Age (years old)	59.7 ± 12.7	56.8 ± 14.5	0.038*
Current weight (kg)	62.7 ± 15.3	70.0 ± 15.9	0.000**
Disease duration (months)	11.1 ± 12.0	11.7 ± 10.7	0.594
Height (m)	1.6 ± 1.0	1.6 ± 1.0	0.303
Current BMI (kg m^{-2})	23.0 ± 5.2	25.7 ± 5.1	0.000**
Weight loss (Kg)	11.6 ± 7.2	-1.2 ± 4.2	0.000**
Habitual weight (kg)	74.3 ± 16.4	68.8 ± 15.9	0.001*
Habitual BMI (kg m^{-2})	27.2 ± 5.4	25.4 ± 4.9	0.001*

Note: m = Meters; kg = kilos; Student's T-test; *Significant difference at 5%; **Significant difference at 1%. Source: Elaborated by the authors

Data were grouped according to gender, and patients who presented lower severe WL were majority men ($p < 0.005$). Patients with BMI indicating overweight and obesity were in greater quantity in the group of individuals with not severe WL, in comparison to the group of individuals with severe WL ($p < 0.05$). Tumor localization was compared to WL, and the results demonstrated that most of the patients with GI tract tumor presented severe WL when compared to patients with other tumors ($p < 0.005$) (Table 6).

Table 6. Comparison between patients with severe and not severe weight loss regarding age range, gender, current BMI and tumor localization, 2017.

Parameter	% Severe WL No. (%)	% Not severe WL No. (%)	p
Age			
Adult	102 (44.9)	92 (52.6)	
Elderly	125 (55.1)	83 (47.4)	0.133
Gender			
Female	114 (50.2)	113 (64.6)	
Male	113 (49.8)	62 (35.4)	0.004*
Current BMI			
Malnutrition	75 (33.0)	24 (13.7)	
Eutrophia	98 (43.2)	65 (37.1)	
Overweight/Obesity	54 (23.8)	86 (49.1)	0.000**
Tumor localization			
Head and Neck	37 (16.3)	15 (8.6)	
Breast	28 (12.3)	63 (36.0)	
GI tract	85 (37.4)	33 (18.9)	0.000**
Lung	26 (11.5)	15 (8.6)	
Others	51 (22.5)	49 (28.0)	

Note: Nº. = Number; GI tract = gastrointestinal tract; BMI = Body mass index; Chi-squared test;*Significant difference at 5%; **Significant difference at 1%. Source: Elaborated by the authors

Discussion

In general, the average age of the studied population was 58.5 ± 13.6 years old. Even without a statistical difference, 51.7% of the sample was composed of elderlies. Recent researches indicate that the prevalence of individuals with 50-74 years old represent 53% of all new cases of cancer and, elderly people with more than 75 years old represent more than a third (Cancer Research UK [CR], 2016). Studies demonstrate 40% of new cases of cancer diagnosed in the elderly population are prostate, colorectal, lung, bladder, pancreas and stomach cancers (Clèries et al., 2018).

In the population studied, the prevalence was of women (56.5%). When it comes to oncological patients, the individual's gender influence significantly, being men the most affected (CR, 2016). The types of cancer that affect men more frequently are prostate, colon, lung and skin cancers (American Cancer Society [ACS], 2017), and women are often affected by breast, colon, endometrium, lung, skin and ovary cancers (American Cancer Society [ACS], 2015).

The sample with greater severe WL was classified by BMI as with overweight or obesity, which is above 25.0 kg m^{-2} to adults and 28.0 kg m^{-2} to elderlies. The incidence of sarcopenia – muscular mass, weight and strength loss – in patients with overweight or obesity was higher when compared to the rest of the sample. Obesity became a critical risk factor for cancer (Zhang, Liu, Shao & Zheng, 2017). However, ESPEN specialists identified nutritional risk in patients with overweight who had a considerable WL (Cederholm et al., 2017). According to the World Cancer Research Fund (2007), weight gain has been causally associated with an increased risk of developing ten different types of cancer, including, esophagus, colorectal, gallbladder, pancreas, liver, breast, ovary, endometrium, kidney and prostate cancer, which corroborates with Lou et al. (2017) study.

Among all cancer localizations analyzed, GI tract cancer presented significant difference regarding patients' severe WL ($p < 0.05$). In patients with gastric cancer, malnutrition is caused by insufficient ingestion of food due to lack of appetite, dysphagia, dyspeptic symptoms (epigastric pain, nausea, and vomit) and impaired digestion and absorption (Brewczyński et al., 2017).

Malnutrition prevalence associated with severe WL was recently reported, varying from 36 to 43% in a population with gastric and colorectal cancer (Gavazzi, Colatruglio, Sironi, Mazzafero & Miceli, 2011). Malnutrition is an independent risk factor to mortality and morbidity, and patients with a tumor in the superior GI tract are particularly prone to developing malnutrition, due to malabsorption, obstructive symptoms, nausea, epigastralgia, constipation or diarrhea (Lecleire et al., 2006; Mariette, De Botton & Piessen, 2012; Caillet et al., 2017).

Head and neck tumor demonstrate a high prevalence when related to severe and not severe WL, with a discrepancy of 37 and 15 individual. Patients with head and neck cancer often present WL, especially the loss of lean mass and functional performance (Lonkvist et al., 2017). In Webster et al. (2018), study, with a population composed of 666 patients diagnosed with oropharyngeal cancer during the years 2004 to 2017, the patients presented 30,3% WL during oncological treatment.

In our study, the BMI of patients was significantly different, gradually decreasing from 26.4 to 24.2 kg m^{-2} with a consequent average WL of 6.02 kg. The sample of the study presented a decline in weight and, consequently, a decrease in habitual and current BMI from 27.2 to 25.4 kg m^{-2}, respectively. Low BMI and WL percentage, independently, anticipate a global survival rate (Arends et al., 2017), which is a strong predictor of mortality by cancer (Cederholm et al., 2015; Hong, Yi, Yi, Hong, & Ohrr, 2016). However, Cushen et al. (2016) reported that parameters such as BMI do not predict clinical results, because they do not precisely distinguish the loss of lean and fat mass, neither describe each tissue. Brewczyński et al. (2017) reported similar statement.

In the present study, 55.06% of elderlies presented severe WL, which trigger malnutrition, a decline in life quality, increased mortality, low tolerance to oncologic treatment and poor chemotherapy efficiency (Gioulbasanis et al., 2011; Aaldriks et al., 2013; Soubeyran et al., 2012; Hong et al., 2016). However, a prospective Italian study with 1556 cancer patients, demonstrated that 689 individuals were above 65 years old and presented an average WL of 9.5%, in addition, the percentage of patients with severe WL was of 42.5% (Mariani et al., 2012).

In a research made with 153 patients in the Oncological Medicine University of Turkey, the patients were diagnosed with colorectal (51.6%), gastric (26.8%), pancreatic (11.8%), hepatic (7.2%), biliary tract (2%) and esophagus (0.7%) cancer. 37.9% of those patients presented malnutrition, 34.6% were at risk of malnutrition, and only 27.5% were considered nourished (Bicakli et al., 2017).

The consequences of malnutrition include the impairment of immune functions and functional performance, delay in wound healing, muscular loss, an increase of toxicity induced by chemotherapy and decreased response to the treatment (Van Cutsem & Arends, 2005; Bozzetti, 2015). Therefore, researchers state that WL is an essential predictor of oncological malnutrition (Zhang et al., 2018), which trigger poor quality of life and a higher rate of mortality (Quinten et al., 2009).

Conclusion

Finally, it's important to prioritize the follow-up of patients with clinical-pathological factors that cause weight loss, iIn order to provide a higher quality of life and lower risk of mortality.

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