Gastrointestinal changes during nutritional follow-up of cancer patients undergoing outpatient chemotherapy

Laiz **SARAGIOTTO**, Vânia Aparecida **LEANDRO-MERHI**, José Luis Braga de **AQUINO** and José Alexandre **MENDONÇA**

Received: 13 January 2020 Accepted: 7 August 2020

ABSTRACT – Background – Cancer patients may have gastrointestinal changes that influence nutritional status. **Objective** – To investigate the occurrence of gastrointestinal changes resulting from outpatient chemotherapy treatment in cancer patients. **Methods** – In a retrospective longitudinal study, the nutritional status and chemotherapy gastrointestinal changes (nausea, vomit, diarrhea, constipation, mucositis, dysphagia, xerostomia, inappetence, dysgeusia and heartburn) in cancer patients (n=187) were investigated in an outpatient follow-up. For the study of the parameters over time, the generalized estimating equation (GEE) method was used. Kruskal-Wallis, Mann-Whitney tests and Spearman coefficient, at a significance level of 5% were also used. **Results** – The majority of the patients were female (63.64%) and the mean age was 57.5±12.1 years. The most frequent symptoms were nausea (18.54%); inappetence (18.31%); intestinal constipation (11.58%); diarrhea (7.98%); xerostomia (7.59%) and vomiting (7.43%). The nutritional status did not exhibit any relevant changes (*P*=0.7594). However, a higher prevalence of eutrophy was observed, followed by overweight; vomiting exhibited a significant difference (*P*=0.0211). The nausea symptom exhibited a significant difference with a higher prevalence of colorectal neoplasia when compared to breast neoplasia (*P*=0.0062); as well as vomiting in lung and colorectal neoplasias (*P*=0.0022), and dysphagia, in head and neck neoplasia, when compared to other neoplasms (*P*<0.001). There was a statistically significant difference between the number of medical appointments and gender (*P*=0.0102) and between dysphagia and gender (*P*<0.0001). **Conclusion** – The study findings enhance the need for signs and symptoms follow up, as well as nutritional status follow up of patients undergoing outpatient chemotherapy.

HEADINGS – Gastrointestinal diseases. Nutritional status. Neoplasms. Adjuvant chemotherapy.

INTRODUCTION

Cancer patients on chemotherapy may often experience a few side effects from treatment, which may influence nutritional status⁽¹⁻⁴⁾.

A systematic review by Caillet et al. 2017⁽³⁾ investigated the association between cachexia, chemotherapy and outcomes in elderly cancer patients. During the course of chemotherapy, the authors found a weight loss among 40%–91.6% of patients, depending on the location of the tumor⁽³⁾. This systematic review also showed that the most frequently observed symptoms were dry mouth, nausea, diarrhea, and intestinal constipation⁽³⁾. Appetite disorders are also prevalent among cancer patients with risk of malnutrition and have a significant impact on the nutritional status and quality of life⁽¹⁾.

In the study conducted by Arribas et al.⁽²⁾, patients with head and neck cancer who underwent chemotherapy were evaluated. As a result, the authors found that 95% of the patients exhibited symptoms of moderate malnutrition, with loss of muscle mass, in addition to prevalence of dysphagia and odynophagia symptoms⁽²⁾. It is very common in cancer patients and in chemotherapeutic processes that a nutritional slump occurs and such result can directly interfere with the patient's quality of life⁽⁵⁻⁸⁾.

However, in a longitudinal study by Salas et al.⁽⁹⁾, cancer patients on chemotherapy did not experience a drop in nutritional status compared to the other parameters reviewed in the study⁽⁹⁾. In a Brazilian study⁽¹⁰⁾, the authors made a systematic review and meta-analysis of randomized clinical trials, showing that the chemotherapy provided an increased survival rate, improved life quality and a more symptom-free period.

In view of the above, the objective of this study was to investigate the occurrence of gastrointestinal changes resulting from outpatient chemotherapy treatment in cancer patients.

METHODS

Study characteristics, inclusion and exclusion criteria and ethical approval

This was a longitudinal retrospective study, developed between 2017 and 2018. The study population included adult and elderly patients of both genders, who had several neoplasms and underwent outpatient chemotherapy at a university hospital through the National Health Service (SUS).

Data collection was performed based on the medical records of patients undergoing outpatient oncologic chemotherapy, only

Declared conflict of interest of all authors: none
Disclosure of funding: no funding received
Programa de Pós-Graduação em Ciências da Saúde, PUC-Campinas, SP, Brasil.
Corresponding author: Vânia Aparecida Leandro-Merhi. E-mail: valm@puc-campinas.edu.br

after approval by the Institution's Ethics and Research Committee (opinion no. 2,251,419). For the eligibility of the population to be studied, adult and elderly patients of both genders were adopted as inclusion criteria for participation in the study; patients with neoplasias, more frequent in the chemotherapy outpatient clinic (breast, lung, colorectal, gynecological and head and neck neoplasms); and who attended regularly outpatient treatment more than four times, within a year. Patients who visited the outpatient clinic less than four times (n=302) and those with less frequent neoplasms (n=84) were excluded from the study.

Thus, out of the 573 patients under outpatient chemotherapy during the study period, 187 patients were recruited for this study, considering all the inclusion and exclusion criteria (FIGURE 1).

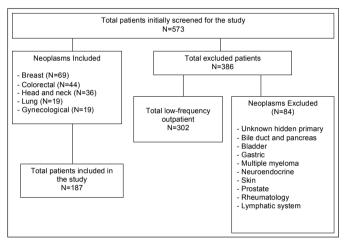


FIGURE 1. Patients enrolled in the study.

Data collection and variables investigated

For the purpose of this study data collection was obtained from the entries in the medical records, since all the routine information of the institution's hospital care is regularly and systematically entered in the patients' medical records under outpatient care at the chemotherapy outpatient clinic. These data were collected through a data collection form previously developed for this investigation, which included demographic data, such as gender, age, date of birth, date and frequency of outpatient visits, diagnosis and type of neoplasia.

Next, anthropometric indicators of weight, height and body mass index (BMI), nutritional status and symptoms and/or side effects experienced during chemotherapy were collected. Nutritional status was assessed using the BMI classification. The criteria established by the World Health Organization (2000)⁽¹¹⁾ for adults and the criteria established by Lipschitz⁽¹²⁾ for the elderly were taken into account to classify the BMI. The weight evolution of patients during all outpatient appointments, from the first day of care to the other visits performed was also assessed.

Subsequently, a survey of all the symptoms and/or side effects exhibited by the patients during treatment such as nausea, vomiting, diarrhea, constipation, mucositis, dysphagia, xerostomia, inappetence, dysgeusia and pyrosis were performed.

Statistical evaluation

Data were tabulated using Excel® software and the statistical analysis was performed with the aid of the SAS program⁽¹³⁾. For the characterization of the sample, a descriptive analysis was

performed, with frequency tables for categorical variables, position and dispersion measurements for continuous variables (mean values, standard deviation, median, minimum and maximum). For the study of the parameters over time, the Generalized Estimating Equation (EEG) method was used⁽¹⁴⁾. The estimates were calculated by maximum likelihood in order to weight the difference in the number of repetitions of each patient. The Kruskal-Wallis test was used to compare the numerical measures summarized among the five different groups of neoplasia. If this test was significant, the Dunn test was applied when necessary, in order to analyze which of the five groups exhibited different values⁽¹⁵⁾. For the comparison of numerical measures between the two groups, the Mann-Whitney test was used. The Spearman coefficient was applied to analyze the relationship between two variables with numerical measures. The level of significance adopted for the statistical tests was 5%⁽¹⁶⁾.

RESULTS

This study showed that outpatient visits occurred 1,278 times, since the same patient made visits more than four times.

In the study population (n=187), 36.90% (n=69) of the patients exhibited breast neoplasia; 23.53% (n=44) exhibited colorectal neoplasia; 19.25% (n=36) had head and neck neoplasia; 10.16% (n=19) had gynecological neoplasia and 10.16% (n=19) lung neoplasia. The majority of the patients studied were female (63.64%, n=119) while 36.36% (n=68) were males. The mean age of the study population was 57.5±12.1 years. With regard to the symptoms exhibited by cancer patients during outpatient chemotherapy, the most prevalent symptoms were nausea (18.54%, n=237); inappetence (18.31%, n=234); constipation (11.58%, n=148); diarrhea (7.98%, n=102); xerostomia (7.59%, n=97); vomiting (7.43%, n=95); dysgeusia (4.46%, n=57); dysphagia (3.99%, n=51); mucositis (3.6%, n=46) and heartburn (1.8%, n=23). Among the most frequently prescribed nutritional guidelines during outpatient follow-up, 52.10% (n=582) were general type guidelines; 28.20% (n=315) were symptom guidelines; 9.49% (n=106) indicated the use of food supplement; 8.50% (n=95) emphasized the general guidelines; (n=17) were prescribed enteral nutrition and 0.18% (n=2) were conducts with respect to diet consistency (data not shown in tables).

The distribution of symptoms exhibited by the patients in relation to the frequency of consultations was $18.8\pm23.7\%$ with symptom of nausea; $18.0\pm23.2\%$ with inappetence symptom; $12.2\pm18.9\%$ with intestinal constipation symptom; $12.2\pm18.9\%$ with intestinal constipation symptom; $12.2\pm18.9\%$ with symptom of diarrhea; 12.2% with vomiting symptom; 12.2 ± 16.1 with xerostomia symptom; 12.2% with dysgeusia symptom; 12.2% with pyrosis symptom, 12.2% with dysphagia symptom and 12.2% with mucositis symptom (data not shown in tables). The most frequent symptoms in all the visits were 18.5% nausea; 18.31% inappetence, 11.5% intestinal constipation; 12.2% diarrhea; 12.2% vomiting; 12.2% dysgeusia; 12.2% dysphagia; 12.2% naucositis and 12.2% pyrosis (data not shown in tables).

TABLE 1 shows the longitudinal distribution and comparison of changes in nutritional status throughout the visits. In order to perform the statistical analysis, the GEE method was only applied until the 6th visit, due to the significant loss of follow-up of patients throughout the other outpatient visits. When reviewing the studied variables, it was observed that the nutritional status of the patients did not exhibit relevant changes until the 6th visit (P=0.7594). However, it was possible to observe that the eutrophy condition

was most prevalent among the visits, followed by the nutritional status classified as overweight (TABLE 1).

According to the statistical analysis performed by the GEE method applied until the 6th visit, due to loss of follow-up throughout the other visits, TABLE 2 shows that the vomiting symptom was the only symptom that presented a statistically significant difference (P=0.0211).

According to the descriptive analysis and the comparison of the variables studied among the five most frequent types of neoplasms, it was verified that age was one of the variables that did not exhibit a statistically significant difference (TABLE 3). However, when comparing the five types of neoplasms in relation to the symptoms experienced, it was observed that the symptom of nausea exhibited a statistically significant difference, with a higher prevalence in colorectal neoplasia; when compared to breast neoplasia (P=0.0062) (TABLE 3). The symptom of vomiting presented a statistically significant difference in lung and colorectal neoplasms when compared to breast neoplasms (P=0.0022). Just like the symptom of dysphagia, which exhibited a statistically significant difference in head and neck neoplasia when compared to the other neoplasms (P<0.001) (TABLE 3).

FIGURE 1 shows an analysis of the distribution of symptoms exhibited during the first six visits, in the outpatient chemotherapy follow-up, analyzed using the GEE method. There was a statistically significant difference for the symptom of vomiting (P=0.0211). It was also observed that the symptoms of nausea (P=0.7664) and inappetence (P=0.5214) were the most prevalent, although with-

out any statistically significant difference. On the other hand, the symptoms of xerostomia (P=0.4997) and diarrhea (P=0.5410) were the less frequent symptoms reported by the patients and also with no statistically significant difference (FIGURE 2).

FIGURE 3 shows the distribution of percentage of days with each symptom among types of neoplasia. It was observed that the symptoms that stood out most among the five types of neoplasias were nausea, inappetence, constipation and diarrhea. However, with the exception of the symptoms of nausea in colorectal and breast neoplasms; none of the other symptoms exhibited a statistically significant difference.

Other important variables to consider are the symptoms of dysphagia, dysgeusia, pyrosis and mucositis, which occurred with low frequency, related to the five neoplasms studied.

However, the dysphagia symptom was the only one showing a statistically significant difference in head and neck neoplasia, when compared to the other types of cancer (P<0.0001). It was also observed that the symptoms of constipation, dysphagia and nausea were prevalent in at least one patient, during all days of outpatient follow-up.

In the descriptive analysis and comparison of the variables studied between genders, assessed by the Mann-Whitney test, it was observed that there was a statistically significant difference between the number of visits and gender (P=0.0102), as well as between the symptom of dysphagia and gender (P<0.0001). In the other variables studied (other symptoms and age), there was no statistically significant difference when compared with gender.

TABLE 1. Longitudinal distribution and comparison of changes throughout the visits.

| | | Nutritional status | | | | | | | | | | | |
|--------------------------------|------------|--------------------|-----------|--------|------|--------|----|-------|-------|--|--|--|--|
| Number of medical appointments | Low weight | | Eutrophic | | Over | weight | O | | | | | | |
| appointments | N | % | N | % | N | % | N | % | Total | | | | |
| 1st | 29 | 16.86 | 69 | 40.12 | 48 | 27.91 | 26 | 15.12 | 172 | | | | |
| 2nd | 31 | 17.32 | 73 | 40.78 | 47 | 26.26 | 28 | 15.64 | 179 | | | | |
| 3rd | 33 | 18.13 | 71 | 39.01 | 49 | 26.92 | 29 | 15.93 | 182 | | | | |
| 4th | 34 | 20.12 | 64 | 37.87 | 45 | 26.63 | 26 | 15.38 | 169 | | | | |
| 5th | 27 | 20.93 | 49 | 37.98 | 34 | 26.36 | 19 | 14.73 | 129 | | | | |
| 6th | 21 | 23.60 | 33 | 37.08 | 22 | 24.72 | 13 | 14.61 | 89 | | | | |
| 7th | 17 | 26.15 | 22 | 33.85 | 17 | 26.15 | 9 | 13.85 | 65 | | | | |
| 8th | 10 | 20.83 | 14 | 29.17 | 16 | 33.33 | 8 | 16.67 | 48 | | | | |
| 9th | 11 | 27.50 | 10 | 25.00 | 14 | 35.00 | 5 | 12.50 | 40 | | | | |
| 10th | 7 | 24.14 | 6 | 20.69 | 13 | 44.83 | 3 | 10.34 | 29 | | | | |
| 11th | 6 | 31.58 | 2 | 10.53 | 9 | 47.37 | 2 | 10.53 | 19 | | | | |
| 12th | 7 | 38.89 | 1 | 5.56 | 8 | 44.44 | 2 | 11.11 | 18 | | | | |
| 13th | 3 | 25.00 | 1 | 8.33 | 6 | 50.00 | 2 | 16.67 | 12 | | | | |
| 14th | 3 | 27.27 | 2 | 18.18 | 6 | 54.55 | 0 | 0 | 11 | | | | |
| 15th | 2 | 25.00 | 2 | 25.00 | 4 | 50.00 | 0 | 0 | 8 | | | | |
| 16th | 2 | 28.57 | 2 | 28.57 | 3 | 42.86 | 0 | 0 | 7 | | | | |
| 17th | 0 | 0 | 2 | 40.00 | 3 | 60.00 | 0 | 0 | 5 | | | | |
| 18th | 0 | 0 | 1 | 33.33 | 2 | 66.67 | 0 | 0 | 3 | | | | |
| 19th | 0 | 0 | 1 | 33.33 | 2 | 66.67 | 0 | 0 | 3 | | | | |
| 20th | 0 | 0 | 1 | 33.33 | 2 | 66.67 | 0 | 0 | 3 | | | | |
| 21th | 0 | 0 | 2 | 66.67 | 1 | 33.33 | 0 | 0 | 3 | | | | |
| 22th | 0 | 0 | 1 | 100.00 | 0 | 0 | 0 | 0 | 1 | | | | |
| 23th | 0 | 0 | 1 | 100.00 | 0 | 0 | 0 | 0 | 1 | | | | |
| Total | 2 | 43 | 2 | 430 | 3 | 351 | 1 | .72 | 1,196 | | | | |

P=0.7594; by the Generalized Estimating Equation (GEE)

TABLE 2. Longitudinal comparison of the most frequent symptoms exhibited by patients over time.

| Number | Symptoms | | | | | | | | | | | | | | | | | |
|--------------|----------|--------|-------|-------|-------|----------|----|--------------|-------|----|------------|-------|----|-------------|-------|----|--------|-------|
| of medical | Nausea | | | Vomit | | Diarrhea | | Constipation | | | Xerostomia | | | Inappetence | | | | |
| appointments | N | % | Total | N | % | Total | N | % | Total | N | % | Total | N | % | Total | N | % | Total |
| 1st | 37 | 19.79 | 187 | 14 | 7.49 | 187 | 11 | 5.88 | 187 | 27 | 14.44 | 187 | 18 | 9.63 | 187 | 37 | 19.79 | 187 |
| 2nd | 37 | 19.79 | 187 | 23 | 12.3 | 187 | 19 | 10.16 | 187 | 30 | 16.04 | 187 | 13 | 6.95 | 187 | 30 | 16.04 | 187 |
| 3rd | 40 | 21.29 | 187 | 17 | 9.09 | 187 | 19 | 10.16 | 187 | 24 | 12.83 | 187 | 16 | 8.56 | 187 | 31 | 16.58 | 187 |
| 4th | 32 | 17.11 | 187 | 12 | 6.42 | 187 | 15 | 8.02 | 187 | 21 | 11.23 | 187 | 15 | 8.02 | 187 | 41 | 21.93 | 187 |
| 5th | 25 | 17.86 | 140 | 12 | 8.57 | 140 | 12 | 8.57 | 140 | 16 | 11.43 | 140 | 13 | 9.29 | 140 | 25 | 17.86 | 140 |
| 6th | 21 | 21.65 | 97 | 3 | 3.09 | 97 | 10 | 10.31 | 97 | 9 | 9.28 | 97 | 5 | 5.15 | 97 | 18 | 18.56 | 97 |
| 7th | 15 | 21.43 | 70 | 3 | 4.29 | 70 | 5 | 7.14 | 70 | 6 | 8.57 | 70 | 5 | 7.14 | 70 | 15 | 21.43 | 70 |
| 8th | 11 | 21.57 | 51 | 3 | 5.88 | 51 | 4 | 7.84 | 51 | 4 | 7.84 | 51 | 2 | 3.92 | 51 | 8 | 15.69 | 51 |
| 9th | 6 | 14.63 | 41 | 5 | 12.2 | 41 | 2 | 4.88 | 41 | 3 | 7.32 | 41 | 2 | 4.88 | 41 | 8 | 19.51 | 41 |
| 10th | 5 | 16.67 | 30 | 2 | 6.67 | 30 | 2 | 6.67 | 30 | 2 | 6.67 | 30 | 3 | 10.0 | 30 | 6 | 20.00 | 30 |
| 11th | 3 | 13.04 | 23 | 0 | 0 | 23 | 2 | 8.70 | 23 | 1 | 4.35 | 23 | 2 | 8.70 | 23 | 5 | 21.74 | 23 |
| 12th | 3 | 15.79 | 19 | 1 | 5.26 | 19 | 1 | 5.26 | 19 | 2 | 10.53 | 19 | 1 | 5.26 | 19 | 2 | 10.53 | 19 |
| 13th | 1 | 8.33 | 12 | 0 | 0 | 12 | O | 0 | 12 | 1 | 8.33 | 12 | 1 | 8.33 | 12 | 2 | 16.67 | 12 |
| 14th | 1 | 9.09 | 11 | 0 | 0 | 11 | O | 0 | 11 | 1 | 9.09 | 11 | 0 | 0 | 11 | 2 | 18.18 | 11 |
| 15th | 0 | 0 | 8 | 0 | 0 | 8 | O | 0 | 8 | 1 | 12.5 | 8 | 1 | 12.5 | 8 | 3 | 37.5 | 8 |
| 16th | 0 | 0 | 7 | 0 | 0 | 7 | O | 0 | 7 | 0 | 0 | 7 | 0 | 0 | 7 | 0 | 0 | 7 |
| 17th | 0 | 0 | 6 | 0 | 0 | 6 | O | 0 | 6 | 0 | 0 | 6 | 0 | 0 | 6 | 0 | 0 | 6 |
| 18th | 0 | 0 | 4 | 0 | 0 | 4 | O | 0 | 4 | 0 | 0 | 4 | 0 | 0 | 4 | 0 | 0 | 4 |
| 19th | 0 | 0 | 3 | 0 | 0 | 3 | O | 0 | 3 | 0 | 0 | 3 | 0 | 0 | 3 | 0 | 0 | 3 |
| 20th | 0 | 0 | 3 | 0 | 0 | 3 | 0 | 0 | 3 | 0 | 0 | 3 | 0 | 0 | 3 | 1 | 33.33 | 3 |
| 21th | 0 | 0 | 3 | 0 | 0 | 3 | 0 | 0 | 3 | 0 | 0 | 3 | 0 | 0 | 3 | 0 | 0 | 3 |
| 22th | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 1 |
| 23th | 0 | 0 | 1 | 0 | 0 | 1 | O | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 1 |
| Total | | 237 | 1278 | | 95 | 1278 | | 102 | 127 | | 148 | 1278 | | 97 | 1278 | 2 | 234 | 1278 |
| P- value | | 0.7664 | | | 0.021 | 1 | | 0.5410 |) | | 0.6336 | 5 | | 0.4997 | 7 | | 0.5214 | |

Remark: The Generalized Estimating Equation Method (GEE) was only applied until the 6^{th} visit, due to the significant loss of follow-up of the patients, during the other outpatient visits.

TABLE 3. Descriptive analysis and comparison of the variables presented among the 5 types of neoplasia of the patients in outpatient chemotherapy follow-up.

| Neoplasms | | | | | | | | | | | |
|--------------|----------------------|--------|-----------------|----------|-----------------|------------|-----------------|--------|-----------------|----------|--------------|
| Variables | Head and neck (n=37) | | Colorecta | l (n=44) | Gynecologi | cal (n=19) | Breast (| n=69) | Lung (n | P-value* | |
| | Avg. ±DP | Median | Avg. ±DP | Median | Avg. ±DP | Median | Avg. ±DP | Median | Avg. ±DP | Median | |
| Age | 58.6 ±12.4 | 60.0 | 60.4±9.3 | 61.0 | 57.2±15.2 | 62.0 | 54.9 ± 12.8 | 57.0 | 58.4 ± 10.4 | 61.0 | 0.2767 |
| Visits | 6.7 ± 2.9 | 5.0 | 7.1 ± 4.6 | 5.0 | 6.1 ± 2.5 | 6.0 | 7.2 ± 3.5 | 6.0 | 5.6 ± 1.9 | 5.0 | 0.2412 |
| Nausea | 14.7 ± 21.3 | 0.0 | 25.6±22.5 | 25.0 | 23.3 ± 29.5 | 0.0 | 13.4 ± 21.8 | 0.0 | 25.0 ± 26.2 | 25.0 | 0.0062^{1} |
| Vomiting | 7.5 ± 14.3 | 0.0 | 12.0 ± 15.6 | 2.2 | 9.3 ± 15.1 | 0.0 | 4.4 ± 13.0 | 0.0 | 14.6 ± 20.3 | 0.0 | 0.0022^{2} |
| Diarrhea | 6.7 ± 11.9 | 0.0 | 13.5 ± 20.3 | 0.0 | 8.3 ± 11.9 | 0.0 | 7.8 ± 17.8 | 0.0 | 7.0 ± 13.7 | 0.0 | 0.3687 |
| Constipation | 15.8 ± 22.5 | 0.0 | 9.3 ± 13.7 | 0.0 | 11.2 ± 14.3 | 0.0 | 10.5 ± 18.5 | 0.0 | 19.7 ± 24.8 | 11.1 | 0.4055 |
| Mucositis | 8.7 ± 17.1 | 0.0 | 3.3 ± 9.8 | 0.0 | 2.4 ± 7.4 | 0.0 | 3.9 ± 11.4 | 0.0 | 2.4 ± 7.1 | 0.0 | 0.1586 |
| Dysphagia | 19.1 ± 25.8 | 10.0 | 1.0 ± 4.8 | 0.0 | - | 0.0 | 0.4 ± 2.2 | 0.0 | 4.2 ± 14.3 | 0.0 | $< 0.0001^3$ |
| Xerostomia | 11.1 ± 19.2 | 0.0 | 8.4 ± 15.2 | 0.0 | 2.1 ± 6.3 | 0.0 | 7.5 ± 15.7 | 0.0 | 8.6 ± 19.0 | 0.0 | 0.2808 |
| Inappetence | 17.3 ± 22.1 | 10.0 | 18.2 ± 23.7 | 4.3 | 19.0 ± 20.8 | 16.7 | 15.5 ± 22.7 | 0.0 | 27.2 ± 27.1 | 20.0 | 0.3454 |
| Dysgeusia | 4.4 ± 12.3 | 0.0 | 2.5 ± 9.7 | 0.0 | 1.1 ± 4.9 | 0.0 | 5.1 ± 14.4 | 0.0 | 5.3 ± 13.5 | 0.0 | 0.6707 |
| Heartburn | 0.8±3.6 | 0.0 | 1.7±5.5 | 0.0 | 1.1±4.6 | 0.0 | 3.5 ± 10.0 | 0.0 | 0.9 ± 3.8 | 0.0 | 0.3703 |

^{*} Kruskal-Wallis test followed by the Dunn test, to locate the differences; when necessary.

Difference between (Dunn's test): 1 Colorectal CA and breast CA. 2 Lung CA and breast CA; colorectal CA and breast CA. 3 Head and neck CA and Lung CA; head and neck CA and colorectal CA; head and neck CA and gynecological CA.

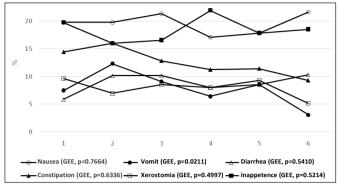


FIGURE 2. Distribution of symptoms during the first six visits. Generalized Estimating Equation (GEE).

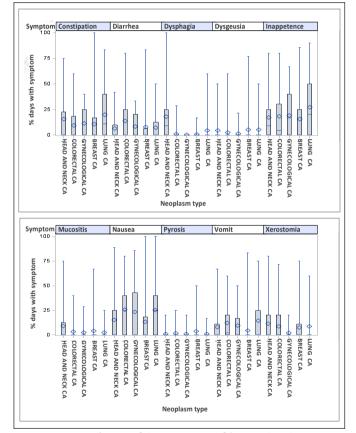


FIGURE 3. Distribution of the percentages of days, with each symptom, among the types of neoplasia. (*Box Plot comparing the percentage of days that each symptom prevailed in the different neoplasms studied).

The correlation between age and percentages of symptoms and number of visits, when analyzed by the Spearman linear correlation coefficient, showed some significant correlations, but all of low intensity. A negative correlation with the symptoms of nausea (-0.15536; *P*=0.0337) and heartburn (-0.16713; *P*=0.0222), and a positive correlation for the mucositis symptom (0.17659; *P*=0.0156) were observed. The other symptoms did not present significant correlations. There was no statistically significant difference in the analysis between nutritional status and the most frequent symptoms (TABLE 4).

TABLE 4. Relation between age and percentage of symptoms and number of medical appointments analyzed by Spearman's linear correlation coefficient.

| W | Age | | | | |
|--------------------------------|-----------|----------|--|--|--|
| Variables | Spearman* | P- value | | | |
| Number of medical appointments | 0.11259 | 0.1250 | | | |
| Nausea | -0.15536 | 0.0337 | | | |
| Vomiting ou vomit | -0.06910 | 0.3474 | | | |
| Diarrhea | -0.04307 | 0.5583 | | | |
| Constipation | 0.01358 | 0.8537 | | | |
| Mucositis | 0.17659 | 0.0156 | | | |
| Dysphagia | 0.13699 | 0.0615 | | | |
| Xerostomia | -0.00405 | 0.9562 | | | |
| Inappetence | 0.13431 | 0.0669 | | | |
| Dysgeusia | -0.02039 | 0.7818 | | | |
| Heartburn | -0.16713 | 0.0222 | | | |

^{*} Spearman linear correlation coefficient.

DISCUSSION

In this study, 36.90% were patients with breast neoplasia; 23.53% with colorectal neoplasia and 19.25% with head and neck neoplasia. A study by Coa et al.⁽¹⁷⁾, carried out in seven specialized cancer centers in the United States, enrolled 1,199 patients, 17.3% of whom suffered from breast neoplasia. The study also found that 12.9% of the patients had gastrointestinal neoplasia, 10.8% had lung neoplasms, 24.2% had other types of neoplasms, and 19.9% had hematologic malignancies. In addition, 59.8% of the patients were female⁽¹⁶⁾; these data come close to the data found in this study.

In this study, a few symptoms were frequently reported by the patients. Those that stood out were nausea, followed by intestinal constipation and inappetence. Different results were found in a study conducted by Arrieta; Nunez and Reynoso⁽¹⁸⁾, in which the most prevalent symptoms were diarrhea and mucositis in Mexican patients⁽¹⁸⁾.

When comparing the five neoplasms studied with the most prevalent symptoms, head and neck neoplasia exhibited the symptom of dysphagia with a statistically significant difference (P<0.0001). These findings are similar to those of the study by Felice, et al. (19), in which head and neck neoplasia was also associated with the symptom of dysphagia (19). This review study conducted by Italian researchers (Felice et al. (19)) pointed out that one of the reasons for direct interference in dysphagia symptom frequency in patients with head and neck neoplasia is late radiation. The study indicated the importance of appropriate multidisciplinary treatment for the quality of life of those patients (19).

In the longitudinal analysis of the most frequent symptoms, according to the GEE method, it was observed that the symptom of vomiting was the only symptom that exhibited a statistically significant difference in the colorectal and lung neoplasms when compared to breast neoplasia. Different findings were observed in the study by Eghbali, et al.⁽²⁰⁾, in patients selected from two hospitals located in an urban area of Iran with breast cancer undergoing chemotherapy, who indicated as main complaint the symptom of nausea and vomiting⁽²⁰⁾.

When comparing colorectal neoplasia, a statistically significant difference was observed for the symptom of nausea when compared to breast neoplasia. Different results were found in the study of Oliva, et al.⁽²¹⁾ in Sweden between chemotherapy treatment in women with breast cancer and who exhibited prevalent symptom of nausea⁽²¹⁾.

When analyzing the percentage of days with each symptom in the five neoplasms studied, it was observed that the symptoms of nausea, constipation, inappetence and diarrhea were the most outstanding, but the only one that exhibited a statistically significant difference was the nausea symptom.

A randomized trial conducted by Lai et al. (22) in Hong Kong, assessed the effects of aromatic massage in advanced cancer patients with symptoms of intestinal constipation. The study showed that the constipation symptom was more prevalent in patients with lung neoplasia (56.3%), which tends to match the findings of this study. The authors also exhibited other important findings and concluded that the effects of aromatic massages can positively help patients with neoplasia and constipation (22).

The symptoms of xerostomia and diarrhea were frequent in colorectal neoplasias, but without statistically significant difference. These findings were also similar to those found by Palmieri, et al.⁽²³⁾, in a Brazilian study, who evaluated the acceptance of food preparations and their associations to the symptoms in the treatment of cancer patients, showing that the xerostomia symptom was the most frequent. In our study the symptom of dysphagia was more associated with head and neck neoplasia when compared to other types of neoplasms. In a French observational multicentre cross-sectional study of malnutrition in elderly patients with cancer, Guily et al.⁽²⁴⁾, the most prevalent symptoms were dysgeusia, nausea, vomiting and dysphagia. An American study, from the University of Michigan, conducted by Sapir et al.⁽²⁵⁾, found no correlation of the symptom with the age of patients with oropharyngeal neoplasia.

A review of the literature⁽²⁶⁾, found results that are in agreement with the findings of this study, since among the patients enrolled, the nausea symptom was prevalent. The authors also observed that the nausea symptom was prevalent in younger patients with low education⁽²⁶⁾.

In many studies, the presence of signs and symptoms is a factor that directly interferes with the nutritional status of cancer patients. In this study, the symptom of vomiting was more prevalent in the eutrophic nutritional status. Data from the study by Lafitte, et al. (27), in a Brazilian hospital, showed prevalence in the eutrophic nutritional status. However, the symptoms of nausea, abdominal distension and constipation were the most prevalent (27).

In the nutritional status of overweight, the symptom that prevailed was that of xerostomia; these findings which oppose a meta-analysis performed by Bressan, et al. (5), in which the xerostomia symptom was found in seven articles reviewed, showing the relationship of xerostomia with weight loss.

Study limitations

In this study, a difficulty was found with regard to the limitations of the retrospective study, associated to difficulties in follow-up and loss of follow-up in the medical records of the studied population. Oda et al.⁽²⁸⁾ conducted a survey in eleven Japanese institutions with patients with gastric neoplasia. As a result, in one year of study, 714 patients exhibited gastric neoplasia conditions; however, 655 were treated periodically. These findings are in agreement with this study, evidencing that loss of follow-up is a relatively common factor in retrospective studies. Another limitation of the present study refers to the fact that socioeconomic data on schooling and income were not investigated, which could assist in the analysis of the results that were found.

CONCLUSION

The symptoms of nausea, inappetence and intestinal constipation were the most frequently observed symptoms and the findings of this study enhance the need for follow-up of signs and symptoms, as well as nutritional status, of patients undergoing outpatient chemotherapy.

ACKNOWLEDGMENTS

We are grateful for the support of the Pontifical Catholic University of Campinas-SP-Brazil.

Authors' contribution

All authors contributed equally to data collection and analysis, and manuscript writing and review. All authors approved the final version of the manuscript.

Orcid

Laiz Saragiotto: 0000-0003-1931-2795.

Vania Aparecida Leandro-Merhi: 0000-0002-2623-6471. José Luis Braga de Aquino: 0000-0002-0604-9054. José Alexandre Mendonça: 0000-0003-1689-6705.

Saragiotto L, Leandro-Merhi VA, Aquino JLB, Mendonça JA. Alterações gastrointestinais durante o acompanhamento nutricional de pacientes oncológicos em acompanhamento ambulatorial de quimioterapia. Arq Gastroenterol. 2020;57(4):354-60.

RESUMO – Contexto – Pacientes oncológicos podem apresentar alterações gastrointestinais que influenciam o estado nutricional. Objetivo – Investigar a ocorrência de alterações gastrointestinais decorrentes do tratamento ambulatorial de quimioterapia, em pacientes oncológicos. Métodos – Num estudo longitudinal retrospectivo, investigou-se o estado nutricional e as alterações gastrointestinais (náuseas, vômito, diarreia, constipação, mucosite, disfagia, xerostomia, inapetência, disgeusia e pirose) de pacientes oncológicos (n=187), em acompanhamento ambulatorial de quimioterapia. Para o estudo dos parâmetros ao longo do tempo, utilizou-se o método das equações de estimação generalizadas (EEG). Também foram utilizados os testes de Kruskal-Wallis, Mann-Whitney e o coeficiente de Spearman, com nível de significância de 5%. Resultados – A maioria dos pacientes era do sexo feminino (63,64%) e a média de idade foi 57,5±12,1 anos. Os sintomas mais frequentes foram náuseas (18,54%); inapetência (18,31%); constipação intestinal (11,58%); diarreia (7,98%); xerostomia (7,59%) e vômito (7,43%). O estado nutricional não apresentou alterações relevantes (*P*=0,7594). No entanto, observou-se maior prevalência de eutrofia, seguido do sobrepeso e o vômito apresentou diferença significativa (*P*=0,0211). O sintoma de náusea apresentou diferença significativa com maior prevalência na neoplasia colorretal, quando comparado à neoplasia de mama (*P*=0,0062); assim como o vômito nas neoplasias de pulmão e colorretal (*P*=0,0022). E a disfagia, na neoplasia de cabeça e pescoço, quando comparada às demais neoplasias (*P*<0,001). Houve diferença estatisticamente significante entre o número de consultas médicas e sexo (*P*=0,0102) e entre disfagia e sexo (*P*<0,0001). Conclusão – Os achados encontrados no estudo permitem reforçar a necessidade do acompanhamento de sinais e sintomas, bem como do estado nutricional, de pacientes em acompanhamento ambulatorial de quimioterapia.

DESCRITORES - Gastroenteropatias. Estado nutricional. Neoplasias. Quimioterapia adjuvante.

REFERENCES

- Galindo DEB, Vidal-Casariego A, Calleja-Fernandez A, Hernandez-M A, Maza BP, Lorenzo MP, et al. Appetite disorders in cancer patients: Impact on nutritional status and quality of life. Appetite. 2017;114:23-7.
- Arribas L, Hurtol L, Taberna M, Peiró I, Vilajosana E, Lozano A, et al. Nutritional changes in patients with locally advanced head and neck cancer during treatment. Oral Oncol. 2017;71:67-74.
- Caillet P, Liuu E, Simon AR, Bonnefoy M, Guerin O, Berrut G, et al. Association between cachexia, chemotherapy and outcomes in older cancer patients: A systematic review. Clin Nutr. 2017;36:1473-82.
- Bloechl-Daum B, Deuson, RR, Mavros P, Hansen M, Herrstedt J. Delayed Nausea and Vomiting Continue to Reduce Patients' Quality of Life After Highly and Moderately Emetogenic Chemotherapy Despite Antiemetic Treatment. J Clin Oncol. 2006;24:2276-8.
- Bressan V, Stevanin S, Bianchi M, Aleo G, Bagnasco A, Sasso L. The effects of swallowing disorders, dysgeusia, oral mucositis and xerostomia on nutritional status, oral intake and weight loss in head and neck cancer patients: A systematic review. Cancer Treat Rev. 2016;45:105-19.
- Wilkes PA, Allen D. Nutrition Care: Managing Symptoms From Cancer. The Journal of Nurse Practitioners 2018; 14 (4): 267-275. DOI: https://doi.org/10.1016/j.nurpra.2018.01.011
- Zhang L, Lu Y, Fang Y. Nutritional status and related factors of patients with advanced gastrointestinal cancer. Br J Nutr. 2014;111:1239-44.
- Hackbarth L, Machado J. [Nutritional status of patients treating gastrointestinal câncer]. [Article in Portuguese]. Rev Bras Nutr Clin. 2015;30(4):271-5.
- Salas S, Mercier S, Moheng B, Olivet S, Garcia M, Hamon S, et al. Nutritional status and quality of life of cancer patients needing exclusive chemotherapy: a longitudinal study. Health Qual Life Outcomes. 2017;15(1):1-7.
- Casaretto L, Sousa PL, Mari JJ. Chemotherapy versus support cancer treatment in advanced gastric cancer: a meta-analysis. Braz J Med Biol Res. 2006;39:431-40.
- World Health Organization (WHO). Obesity: Preventing and managing the global epidemic- Report of a WHO Consultation on Obesity. Geneva: Who, 2000.
- Lipschitz DA. Screening for nutritional status in the elderly. Prim Care. 1994; 21:55-67.
- SAS System for Windows (Statistical Analysis System), versão 9.4. Institute Inc, 2002-2012, Cary, NC, USA.
- Stokes ME, Davis CS, Koch GG. Categorial data analysis using the SAS System. Cary: SAS Institute, 1996.
- Allison PD. Handling Missing data by maximum likelihood. Statistical Horizons, Haverford, PA, USA, 2012.

- Conover WJ. Practical Nonparametric statistics. J. Wiley and Sons Inc., New York 1971, 462 S. https://doi.org/10.1002/bimj.19730150311.
- Coa KL. The Impact of Cancer Treatment on the Diets and food preferences of patient receiving outpatient treatment. Nutr Cancer. 2015;67:339-53.
- Arrieta O, Nunez VC, Reynoso EL. Health relates quality of life in patients with lung cancer: Mexican- Spanish version and association with prognosis of the EORTC QLQ- LC13 questionnaire. Lung Cancer. 2012;77:205-11.
- Felice, F, Vicentis M, Luzzi V, Magliulo G, Tombolini M, Ruoppolo G, Polimeni A. Late radiation-associates dysphagia in head and neck cancer patients: evidence, research and management. Oral Oncol. 2018;77:125-30.
- Eghbali M, Yekaninejad MS, Varaei S, Jalalinia SF, Samimi MA, Sa'archi K. The
 effect of auricular acupressure on nausea and vomiting caused by chemotherapy
 among breast cancer patients. Complement Ther Clin Pract. 2016;24:189-94.
- Oliva D, Nilsson M, Bengt-ake A, Lena S, Lewin F, Lewin N. Single Nucleotide polymorphisms might influence chemotherapy induced nausea in woman with breast cancer. Clin Transl Radiat Oncol. 2017;2:1-6.
- 22. Lai TKT, Cheung CK, Fung YH, Tong M, Yau CC. Effectiveness of aroma massage on advanced cancer patients with constipation: a pilot study. Complement Ther Clin Pract. 2011;17:37-43.
- Palmieri BN, Moulatlet EM, Buschinelli LKO, Silva MEMP. Aceitação de preparações e sua associação com os sintomas decorrentes do tratamento de câncer em pacientes de uma clínica especializada. Cad Saúde Colet. 2013;21:2-9. https://doi.org/10.1590/S1414-462X2013000100002.
- Guily JLS, Bouvard E, Raynard B, Goldwasser F, Maget B, Pprevost A, et al. NutriCancer: A French observational multicenter cross-sectional study of malnutrition on elderly patients with cancer. J Geriatr Oncol. 2018;6:74-80.
- Sapir ES, Tao Y, Feng F, Samuls S, Naga IE, Kinch CA, et al. Predictors of Dysgeusia in patients with oropharyngeal cancer treated with chemotherapy and intensity modulated radiations therapy. Int J Radiat Oncol Biol Phys. 2016;96: 354-36.
- Singh KP, Dhruva A.A, Flowers E, Kober KM, Miaskowski C. A review of the literature on the relationships between genetic polymorphisms and chemotherapyinduced nausea and vomiting. Crit Rev Oncol Hematol. 2018;121:51-61.
- Laffitte, AM, Polakiwski, CB, Kato M. Early oral feeding on oncology patients submitted to gastrectomy for gastric cancer. Arq Bras Cir Dig. 2015;28:200-13.
- Oda I, Saito D, Tada M, Iishi H, Tanabe S, Oyama T, et al. A multicenter retrospective study of endoscopic resection for erly gastric cancer. Gastric Cancer. 2006;9:262-70.

