

ORIGINAL ARTICLE

# Quality of life and associated factors in patients with hematological cancer according to EORTC QLQ-C30

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**Abstract**

**Introduction:** hematological cancers account for 9% of all cancers and their progression and treatment directly affect quality of life (QoL).

**Objective:** this study assessed QoL and associated factors in patients with hematological cancer according to the EORTC QLQ-C30.

**Methods:** cross-sectional study carried out from August 2017 to June 2019. We included adults and the elderly of both sexes, with hematological cancer, undergoing oral or venous chemotherapy. Nutritional status was assessed by the Patient-Generated Subjective Global Assessment (PG-SGA) and QoL by EORTC QLQ-C30.

**Results:** fifty-one patients aged in average  $60.0 \pm 15$  years were evaluated. Of these, 51.0% were women, 80.4% were non-white, 37.3% had B lymphoid cell neoplasia, 60.8% had been diagnosed for  $\leq 3$  years, 77.1% were on chemotherapy, and 64.7% were well-nourished. The scores for global health status and functional scales were high and for symptoms and single items they were low, indicating good QoL and functionality and low symptomatology. After multivariate linear regression, the time of diagnosis  $\leq 3$  years was associated with functional performance ( $p < 0.05$ ) and malnutrition was associated with cognitive function ( $p < 0.05$ ) and with symptoms of fatigue, nausea and vomiting, and insomnia ( $p < 0.05$ ).

**Conclusions:** quality of life and functionality considered adequate were observed. Time of diagnosis and malnutrition were the variables that were associated with physical and cognitive function and with the presence of fatigue, nausea and vomiting and insomnia, according to the EORTC QLQ-C30.

**Keywords:** Malnutrition, cancer, nutritional assessment, functional performance, cognition.

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## Authors summary

### Why was this study done?

The study was carried out to meet the demand of the sector responsible for medicating patients from Hematology/Oncology outpatient clinics and to contribute scientifically, since studies on quality of life in patients with hematologic cancer are limited.

### What did the researchers do and find?

The researchers evaluated the quality of life of patients with hematologic cancer undergoing chemotherapy and found in general, good quality of life and functionality, few symptoms and good nutritional status.

### What do these findings mean?

Such discoveries contribute to the scientific community and to the care service for patients with hematological cancer undergoing chemotherapy, since it portrays the quality of life of patients undergoing chemotherapy, enabling corrective and appropriate intervention for the patient.

## INTRODUCTION

Cancer represents an increased burden for the general population due to its high prevalence and consequences for morbidity, mortality, and quality of life<sup>1</sup>. Cancer has become a leading cause of death worldwide, increasing exponentially over the past few decades<sup>2</sup>. For 2020, the estimate of the World Health Organization was of more than 19 million new cases<sup>3</sup>. The incidence of hematological cancer is increasing in economically developed regions, corresponding to 9% of all cancers and being the fourth most frequent type in men and women<sup>4</sup>.

Hematological cancer affects the blood, bone marrow and lymphatic system, constituting a set of diseases that includes leukemias, B lymphoid cell neoplasms, myeloproliferative neoplasms, Hodgkin's lymphomas, and non-Hodgkin's lymphomas<sup>4,5</sup>. Both the disease and its treatments cause many physical, psychological, and social adverse effects, which directly affect the Quality of Life (QoL) of patients<sup>2,6</sup>.

Quality of life involves the individual's perception of their position in life in various spheres such as expectations, standards, concerns and capacities, reflecting functional status, emotional and social well-being, as well as general health. Measuring quality of life has become relevant to analyze the results obtained in the treatment of cancer patients from its perspective<sup>7-9</sup>. As it is influenced by several factors, QoL assessment can contribute to a broader and more comprehensive therapeutic approach that considers the patient's perception<sup>10,11</sup>.

Hinz *et al.*<sup>12</sup> assessed QoL in different types of cancers and observed varying levels of impairment, functionality, and presence of symptoms. When comparing QoL and the functionality of patients with head and neck cancer during and after treatment, Kramer *et al.*<sup>13</sup> identified that these domains had been compromised. However, there was a significant improvement in the following two years of follow-up, showing that treatment can influence QoL.

Cancer treatment can also negatively affect the patient's nutritional status<sup>14</sup>. A good nutritional status increases the response to specific treatments and positively interferes with QoL<sup>6</sup>. In contrast, malnutrition is a major cause of morbidity and responsible for 20% of deaths in cancer patients<sup>1</sup>. Therefore, nutritional intervention is essential to improve nutritional status, signs, and symptoms, and, consequently, QoL<sup>6,14</sup>.

The different factors that influence QoL can be evaluated through the European Organization for Research

and Treatment of Cancer - Quality of Life Questionnaire Core 30 (EORTC QLQ-C30), which aids in the improvement of QoL and successful health resources<sup>15,16</sup>.

Even today, it is necessary and important to assess the nutritional status and QoL of patients with hematological cancer undergoing outpatient chemotherapy, since knowing the profile of these patients enables better nutritional intervention and symptom management. However, there are few studies that considered this population at this stage of treatment, and there is still a lack of answers on which factors are related to QoL at this time.

The objective of this study was to investigate the quality of life and associated factors in patients with hematological cancer according to EORTC QLQ-C30.

## METHODS

### Study Design

This is a descriptive cross-sectional study. At either time, patients were individually invited by a small team, composed of three researchers, to participate in the study. The study protocol was explained and those who agreed to participate signed the Free and Informed Consent Form (CIF).

### Study Location and Period

Carried out in the Antineoplastic and Ambulatory Treatment Unit for hematological cancer at a University Hospital in Vitoria, Espírito Santo. Patients were recruited from August 2017 to June 2019 using convenience sampling and evaluated during chemotherapy sessions or while waiting for a medical appointment.

### Study Population and Eligibility Criteria

Individuals diagnosed with hematologic cancer undergoing chemotherapy treatment. Individuals aged 20 years or over, of both sexes, with clinical diagnosis of hematological cancer and undergoing oral or venous chemotherapy treatment, no matter for how long, answered the questionnaires on nutritional status and QoL. Patients were excluded if they were unable to answer the questionnaire. Individuals aged 20-59.9 years were classified as adults and those aged  $\geq 60$  years were classified as elderly<sup>17</sup>.

## Data Collection

For the study, we developed a specific protocol that included sociodemographic questions, clinical data, and the Patient-Generated Subjective Global Assessment (PG-SGA) and European Organization for Research and Treatment of Cancer (EORTC QLQ-C30) questionnaires. The team responsible for the application of the protocol was properly trained and qualified. Clinical data, such as type of cancer, treatment, and time of diagnosis, were obtained from medical records. The recruited patients were at different times of treatment.

## Nutritional Status Assessment

The Patient-Generated Subjective Global Assessment (PG-SGA) validated for the Brazilian population was used to assess nutritional status. The PG-SGA is divided into two parts: the first addresses issues related to weight, food intake, presence of symptoms of nutritional impact, activities, and function; the second classifies the nutritional status based on the patient's responses, presence of metabolic stress and physical examination. The PG-SGA classification has three stages: well-nourished (A), moderately malnourished or suspected of being so (B), or severely malnourished (C). Patients were divided into two groups: well-nourished (A) and malnourished (B + C)<sup>18</sup>.

## Quality of Life Questionnaire

The QoL questionnaire validated and approved by the European Organization for Research and Treatment of Cancer (EORTC) – EORTC QLQ-C30, version 3.0 – was used to assess the quality of life of patients included in this study (dependent variable)<sup>19</sup>.

The questionnaire has thirty questions divided into multiple- and single-item scales. The multiple-item scales are: Global Health / Quality of Life (QoL); Functional Scale, which is subdivided into five scales: physical function, role performance, emotional function, cognitive function, and social function; Symptom Scale, with symptoms of fatigue, pain, nausea and vomiting and six unique items. For the first twenty-eight questions, the answers range from: nothing (1), little (2), moderate (3) or a lot (4). Questions related to general quality of life were answered on a scale of 1 to 7 (7 = excellent).

The items generate a score ranging from 0 to 100. For Global Health / QoL and the functional scale, a high score represents a high level of quality of life and functioning, respectively. For the symptom scale, a high score indicates a high level of symptoms / problems. The responses were

analyzed according to the EORTC QLQ-C30 Scoring Manual and missing values were imputed according to the method described in the manual<sup>15</sup>.

## Data Analysis

Descriptive analysis was performed, and continuous variables expressed as means and standard deviations, median and percentiles and categorical variables as percentages. The Kolmogorov-Smirnov test was used to verify the normality of the quantitative variables. Non-parametric independent variables were compared using Mann-Whitney and Kruskal-Wallis tests. Parametric independent variables were compared using Student's t test and ANOVA. To determine the influence of variables on the domains and symptoms identified by the EORTC QLQ-C30 (dependent variable), multivariate linear regression analysis with dummy variable was used. There were raw and adjusted values. The adjustment variables were: age, sex, race/color, and type of diagnosis. Variables in which  $p < 0.05$  were included in the association tests. The internal consistency of the Quality-of-Life questionnaire was verified using the Cronbach's Alpha test. The data were analyzed using SPSS® 22.0 software. A significance level of 5.0% was adopted for all tests.

## Ethical and Legal Aspects of the Research

The study was approved by the Research Ethics Committee (CEP) of the Federal University of Espirito Santo, under protocol number 2.141.932.

## RESULTS

The final sample consisted of 51 patients aged in average  $60.0 \pm 15$  years. There was a predominance of women (51.0%), non-whites (80.4%), individuals diagnosed with Lymphoid B Cell Neoplasia (37.3%), time of diagnosis  $\leq 3$  years (60.8%), and oral or venous chemotherapy as the main treatment (77.1%). According to the PG-SGA, most evaluated patients were well-nourished (64.7%).

The results of the EORTC QLQ-C30 are shown in table 1. For global health / QoL, the median was 75.0, indicating good global health status / QoL. The medians of the functional scale domains were high, especially the social function with a median of 100.0, indicating good functioning. The scores on the symptom scale revealed low symptomatology, that is, the presence of symptoms did not compromise quality of life. The symptoms with the highest median values were fatigue and pain. All single items had a median of 0.0.

**Table 1:** EORTC QLQ-C30 Global Health/QoL, Functional and Symptom Scores for patients with hematological cancer

| Variables (n= 51)          | Mean | CI        |
|----------------------------|------|-----------|
| Global health status / QoL | 69.8 | 62.4-77.2 |
| Functional scales          | 68.8 | 63.2-74.4 |
| Physical function          | 70.3 | 64.0-76.6 |
| Role function              | 60.8 | 49.6-72.0 |
| Emotional function         | 77.0 | 69.5-84.5 |

**Continuation - Table 1:** EORTC QLQ-C30 Global Health/QoL, Functional and Symptom Scores for patients with hematological cancer

| Variables (n= 51)      | Mean | CI        |
|------------------------|------|-----------|
| Cognitive function     | 76.5 | 69.4-83.6 |
| Social function        | 73.9 | 64.6-83.1 |
| Symptom scales/items   | 22.1 | 16.4-27.8 |
| Fatigue                | 31.4 | 22.0-40.8 |
| Nausea and vomiting    | 12.1 | 5.5-18.8  |
| Pain                   | 25.2 | 15.8-34.6 |
| Dyspnoea               | 13.7 | 5.3-22.1  |
| Insomnia               | 24.8 | 15.1-34.6 |
| Appetite loss          | 22.9 | 11.9-33.9 |
| Constipation           | 24.2 | 13.4-35.0 |
| Diarrhea               | 5.9  | 1.4-10.4  |
| Financial difficulties | 27.5 | 16.2-38.7 |

CI: Confidence Interval

Quality of life and the functional scale domains of the EORTC QLQ-C30 were compared with different variables (table 2). Patients diagnosed less than three years before had lower averages for physical function (p=0.03) and functional performance (p=0.002). Regarding

nutritional status, the physical function (p=0.04) and cognitive function (p=0.007) domains were reduced in malnourished patients. There were no significant differences for the other variables.

**Table 2:** Comparison of variables with Global Health / QOL and Functional Scale of the EORTC QLQ-C30 of patients with hematological cancer

| Variables        | Global health status/QoL <sup>ac</sup> | Physical function <sup>ac</sup> | Role function <sup>bd</sup> | Emotional function <sup>bd</sup> | Cognitive function <sup>bd</sup> | Social function <sup>bd</sup> |
|------------------|--|---------------------------------|-----------------------------|----------------------------------|----------------------------------|-------------------------------|
|                  | Mean ± SD                              | Mean ± SD                       | Median<br>(P25-P75)         | Median<br>(P25-P75)              | Median<br>(P25-P75)              | Median<br>(P25-P75)           |
| Stage of life    |  |                                 |                             |                                  |                                  |                               |
| Adult (n=21)     | 72.2±26.1                              | 76.0 ± 23.6                     | 66.67<br>(0.00 – 100.00)    | 75.00<br>(8.33 – 100.00)         | 83.33<br>(16.67 – 100.00)        | 66.67<br>(0.00 – 100.00)      |
| Elderly (n=30)   | 68.1±26.8                              | 66.3 ± 20.8                     | 83.33<br>(0.00 – 100.00)    | 91.67<br>(16.67 – 100.00)        | 83.33<br>(16.67 – 100.00)        | 100.00<br>(0.00 – 100.00)     |
| p value          | 0.584                                  | 0.130                           | 0.224                       | 0.197                            | 0.808                            | 0.383                         |
| Gender           |  |                                 |                             |                                  |                                  |                               |
| Male (n=25)      | 68.0 ± 26.2                            | 69.6 ± 21.3                     | 66.67<br>(0.00 – 100.00)    | 91.67<br>(16.67 – 100.00)        | 83.33<br>(33.33 – 100.00)        | 66.67<br>(0.00 – 100.00)      |
| Female (n=26)    | 71.5 ± 29.9                            | 71.0 ± 23.6                     | 83.33<br>(0.00 – 100.00)    | 75.00<br>(8.33 – 100.00)         | 66.67<br>(16.67 – 100.00)        | 100.00<br>(0.00 – 100.00)     |
| p value          | 0.643                                  | 0.830                           | 0.293                       | 0.304                            | 0.443                            | 0.549                         |
| Color            |  |                                 |                             |                                  |                                  |                               |
| White (n=10)     | 63.3 ± 20.9                            | 71.0 ± 21.2                     | 83.33<br>(0.00 – 100.00)    | 70.83<br>(8.33 – 100.00)         | 75.00<br>(16.67 – 100.00)        | 83.33<br>(0.00 – 100.00)      |
| Non-white (n=41) | 71.3 ± 27.5                            | 70.1 ± 22.8                     | 66.67<br>(0.00 – 100.00)    | 83.33<br>(16.67 – 100.00)        | 83.33<br>(16.67 – 100.00)        | 100.00<br>(0.00 – 100.00)     |

**Continuation - Table 2:** Comparison of variables with Global Health / QOL and Functional Scale of the EORTC QLQ-C30 of patients with hematological cancer

| Variables                          | Global health status/QoLac | Physical functionac | Role functionbd           | Emotional functionbd      | Cognitive functionbd       | Social functionbd          |
|------------------------------------|----------------------------|---------------------|---------------------------|---------------------------|----------------------------|----------------------------|
| p value                            | 0.394                      | 0.112               | 0.668                     | 0.149                     | 0.607                      | 0.835                      |
| <b>Diagnosis</b>                   |                            |                     |                           |                           |                            |                            |
| B Cell Lymphoid Neoplasm (n=19)    | 68.4 ± 25.8                | 66.8 ± 22.4         | 66.67<br>(0.00 – 100.00)  | 91.67<br>(25.00 – 100.00) | 100.00<br>(16.67 – 100.00) | 100.00<br>(0.00 – 100.00)  |
| Myeloproliferative Neoplasm (n=13) | 66.0 ± 35.6                | 76.9 ± 20.1         | 100.00<br>(0.00 – 100.00) | 75.00<br>(16.67 – 100.00) | 66.67<br>(50.00 – 100.00)  | 100.00<br>(33.33 – 100.00) |
| Non-Hodgkin's Lymphoma (n=11)      | 75.0 ± 19.0                | 68.6 ± 18.6         | 83.33<br>(0.00 – 100.00)  | 75.00<br>(8.33 – 100.00)  | 66.67<br>(16.67 – 100.00)  | 66.67<br>(0.00 – 100.00)   |
| Others+ (n=8)                      | 71.9 ± 21.8                | 70.0 ± 30.8         | 50.00<br>(0.00 – 100.00)  | 91.67<br>(75.00 – 100.00) | 66.67<br>(33.33 – 100.00)  | 100.00<br>(33.33 – 100.00) |
| p value                            | 0.858                      | 0.656               | 0.526                     | 0.255                     | 0.757                      | 0.529                      |
| <b>Diagnostic time</b>             |                            |                     |                           |                           |                            |                            |
| ≤ 3 years (n=31)                   | 68.8 ± 23.9                | 65.0 ± 22.0         | 33.33<br>(0.00 – 100.00)  | 91.67<br>(8.33 – 100.00)  | 66.67<br>(16.67 – 100.00)  | 100.00<br>(0.00 – 100.00)  |
| > 3 years (n=20)                   | 71.3 ± 30.4                | 78.5 ± 20.5         | 100.00<br>(0.00 – 100.00) | 75.00<br>(16.67 – 100.00) | 91.67<br>(3.33 – 100.00)   | 100.00<br>(0.00 – 100.00)  |
| p value                            | 0.771                      | 0.033               | 0.002                     | 0.253                     | 0.500                      | 0.397                      |
| <b>Treatment Type#</b>             |                            |                     |                           |                           |                            |                            |
| Chemotherapy (n=37)                | 70.7 ± 27.1                | 72.8 ± 21.8         | 83.33<br>(0.00 – 100.00)  | 83.33<br>(8.33 – 100.00)  | 83.33<br>(16.67 – 100.00)  | 100.00<br>(0.00 – 100.00)  |
| Outpatient/RBCC (n=11)             | 67.3 ± 27.7                | 66.3 ± 24.0         | 66.67<br>(0.00 – 100.00)  | 83.33<br>(16.67 – 100.00) | 66.67<br>(33.33 – 100.00)  | 100.00<br>(33.33 – 100.00) |
| p value                            | 0.726                      | 0.402               | 0.713                     | 0.937                     | 0.595                      | 0.243                      |
| <b>PG-SGA</b>                      |                            |                     |                           |                           |                            |                            |
| Well nourished (n=33)              | 72.2 ± 25.6                | 75.0 ± 23.2         | 83.33<br>(0.00 – 100.00)  | 91.67<br>(25.00 – 100.00) | 100.00<br>(33.33 – 100.00) | 100.00<br>(0.00 – 100.00)  |
| Malnourished (n=18)                | 65.3 ± 27.9                | 60.5 ± 19.5         | 66.67<br>(0.00 – 100.00)  | 79.17<br>(8.33 – 100.00)  | 66.67<br>(16.67 – 100.00)  | 83.33<br>(16.67 – 100.00)  |
| p value                            | 0.374                      | 0.040               | 0.684                     | 0.411                     | 0.007                      | 0.502                      |

<sup>a</sup>Student T Test; <sup>b</sup>Mann-Whitey test; <sup>c</sup>Anova; <sup>d</sup>Kruskal Wallis. RBCC: Red blood cell concentrate; PG-SGA: Patient-Generated Subjective Global Assessment; +Others: 5.9%: Hodgkin's lymphoma; 5.9%: Myeloproliferative syndrome; 3.9%: Leukemia. #N=48. Cont.=Continuation.

Table 3 shows the comparison of variables with the symptom scale and unique items. In general, the symptoms did not score high values, indicating that they did not significantly compromise quality of life. When comparing domains by sex, the presence of constipation was higher among women ( $p = 0.034$ ). Patients undergoing outpatient

treatment and with administration of red blood cells had more episodes of insomnia ( $p = 0.029$ ). As for nutritional status, malnourished patients reported more fatigue ( $p = 0.002$ ), nausea and vomiting ( $p = 0.035$ ) and insomnia ( $p = 0.013$ ) when compared to well-nourished patients.

**Table 3:** Comparison of variables with symptoms and unique items of the EORTC QLQ-C30 of patients undergoing hematological cancer treatment

| Variables (N = 51)                 | Fatigue <sup>ab</sup> | Nausea and vomiting <sup>ab</sup> | Pain <sup>ab</sup>    | Dyspnoea <sup>ab</sup> | Insomnia <sup>ab</sup> | Appetite loss <sup>ab</sup> | Constipation <sup>ab</sup> | Diarrhoea <sup>ab</sup> | Financial difficulties <sup>ab</sup> |
|------------------------------------|-----------------------|-----------------------------------|-----------------------|------------------------|------------------------|-----------------------------|----------------------------|-------------------------|--------------------------------------|
|                                    | Median (P25-P75)      | Median (P25-P75)                  | Median (P25-P75)      | Median (P25-P75)       | Median (P25-P75)       | Median (P25-P75)            | Median (P25-P75)           | Median (P25-P75)        | Median (P25-P75)                     |
| Stage of live                      |                       |                                   |                       |                        |                        |                             |                            |                         |                                      |
| Adult (n=21)                       | 33.33 (0.00 – 100.00) | 0.00 (0.00 – 100.00)              | 16.67 (0.00 – 100.00) | 0.00 (0.00 – 66.67)    | 0.00 (0.00 – 100.00)   | 0.00 (0.00 – 100.00)        | 0.00 (0.00 – 100.00)       | 0.00 (0.00 – 66.67)     | 33.33 (0.00 – 100.00)                |
| Elderly (n=30)                     | 22.22 (0.00 – 100.00) | 0.00 (0.00 – 83.33)               | 0.00 (0.00 – 100.00)  | 0.00 (0.00 – 100.00)   | 0.00 (0.00 – 100.00)   | 0.00 (0.00 – 100.00)        | 0.00 (0.00 – 100.00)       | 0.00 (0.00 – 33.33)     | 0.00 (0.00 – 100.00)                 |
| p value                            | 0.760                 | 0.069                             | 0.602                 | 0.989                  | 0.690                  | 0.566                       | 0.398                      | 0.313                   | 0.138                                |
| Gender                             |                       |                                   |                       |                        |                        |                             |                            |                         |                                      |
| Male (n=25)                        | 22.22 (0.00 – 88.89)  | 0.00 (0.00 – 66.67)               | 16.67 (0.00 – 100.00) | 0.00 (0.00 – 100.00)   | 0.00 (0.00 – 100.00)   | 0.00 (0.00 – 100.00)        | 0.00 (0.00 – 100.00)       | 0.00 (0.00 – 66.67)     | 0.00 (0.00 – 100.00)                 |
| Female (n=26)                      | 22.22 (0.00 – 100.00) | 0.00 (0.00 – 100.00)              | 0.00 (0.00 – 100.00)  | 0.00 (0.00 – 100.00)   | 0.00 (0.00 – 100.00)   | 0.00 (0.00 – 100.00)        | 16.67 (0.00 – 100.00)      | 0.00 (0.00 – 66.67)     | 0.00 (0.00 – 100.00)                 |
| p value                            | 0.756                 | 0.052                             | 0.370                 | 0.958                  | 0.750                  | 0.524                       | 0.034                      | 0.659                   | 0.861                                |
| Color                              |                       |                                   |                       |                        |                        |                             |                            |                         |                                      |
| White (n=10)                       | 16.67 (0.00 – 100.00) | 0.00 (0.00 – 100.00)              | 8.33 (0.00 – 100.00)  | 0.00 (0.00 – 100.00)   | 0.00 (0.00 – 100.00)   | 0.00 (0.00 – 100.00)        | 0.00 (0.00 – 100.00)       | 0.00 (0.00 – 33.33)     | 0.00 (0.00 – 100.00)                 |
| Non-white (n=41)                   | 22.22 (0.00 – 100.00) | 0.00 (0.00 – 83.33)               | 16.67 (0.00 – 100.00) | 0.00 (0.00 – 100.00)   | 0.00 (0.00 – 100.00)   | 0.00 (0.00 – 100.00)        | 0.00 (0.00 – 100.00)       | 0.00 (0.00 – 66.67)     | 0.00 (0.00 – 100.00)                 |
| p value                            | 0.667                 | 0.918                             | 0.990                 | 0.458                  | 0.894                  | 0.785                       | 0.567                      | 0.578                   | 0.913                                |
| Diagnosis                          |                       |                                   |                       |                        |                        |                             |                            |                         |                                      |
| B Cell Lymphoid Neoplasm (n=19)    | 22.22 (0.00 – 100.00) | 0.00 (0.00 – 66.67)               | 16.67 (0.00 – 100.00) | 0.00 (0.00 – 100.00)   | 0.00 (0.00 – 100.00)   | 0.00 (0.00 – 100.00)        | 0.00 (0.00 – 100.00)       | 0.00 (0.00 – 33.33)     | 0.00 (0.00 – 100.00)                 |
| Myeloproliferative Neoplasm (n=13) | 22.22 (0.00 – 88.89)  | 0.00 (0.00 – 33.33)               | 16.67 (0.00 – 66.67)  | 0.00 (0.00 – 66.67)    | 33.33 (0.00 – 100.00)  | 0.00 (0.00 – 66.67)         | 0.00 (0.00 – 33.33)        | 0.00 (0.00 – 66.67)     | 0.00 (0.00 – 100.00)                 |

**Continuation - Table 3: Comparison of variables with symptoms and unique items of the EORTC QLQ-C30 of patients undergoing hematological cancer treatment**

| Variables (N = 51)                 | Fatigue <sup>ab</sup> |                      | Nausea and vomiting <sup>ab</sup> |                      | Pain <sup>ab</sup>    |                      | Dyspnoea <sup>ab</sup> |                      | Insomnia <sup>ab</sup> |                      | Appetite loss <sup>ab</sup> |                      | Constipation <sup>ab</sup> |                      | Diarrhoea <sup>ab</sup> |                      | Financial difficulties <sup>ab</sup> |                      |
|------------------------------------|-----------------------|----------------------|-----------------------------------|----------------------|-----------------------|----------------------|------------------------|----------------------|------------------------|----------------------|-----------------------------|----------------------|----------------------------|----------------------|-------------------------|----------------------|--------------------------------------|----------------------|
|                                    | Median (P25-P75)      | Median (P25-P75)     | Median (P25-P75)                  | Median (P25-P75)     | Median (P25-P75)      | Median (P25-P75)     | Median (P25-P75)       | Median (P25-P75)     | Median (P25-P75)       | Median (P25-P75)     | Median (P25-P75)            | Median (P25-P75)     | Median (P25-P75)           | Median (P25-P75)     | Median (P25-P75)        | Median (P25-P75)     | Median (P25-P75)                     | Median (P25-P75)     |
| Myeloproliferative Neoplasm (n=13) | 22.22 (0.00 – 88.89)  | 0.00 (0.00 – 33.33)  | 16.67 (0.00 – 66.67)              | 0.00 (0.00 – 66.67)  | 16.67 (0.00 – 66.67)  | 0.00 (0.00 – 66.67)  | 0.00 (0.00 – 66.67)    | 0.00 (0.00 – 66.67)  | 33.33 (0.00 – 100.00)  | 0.00 (0.00 – 66.67)  | 0.00 (0.00 – 66.67)         | 0.00 (0.00 – 66.67)  | 0.00 (0.00 – 66.67)        | 0.00 (0.00 – 66.67)  | 0.00 (0.00 – 66.67)     | 0.00 (0.00 – 66.67)  | 0.00 (0.00 – 66.67)                  | 0.00 (0.00 – 66.67)  |
| Non-Hodgkin's Lymphoma (n=11)      | 0.00 (0.00 – 100.00)  | 0.00 (0.00 – 100.00) | 0.00 (0.00 – 100.00)              | 0.00 (0.00 – 100.00) | 0.00 (0.00 – 100.00)  | 0.00 (0.00 – 100.00) | 0.00 (0.00 – 100.00)   | 0.00 (0.00 – 100.00) | 0.00 (0.00 – 100.00)   | 0.00 (0.00 – 100.00) | 0.00 (0.00 – 100.00)        | 0.00 (0.00 – 100.00) | 0.00 (0.00 – 100.00)       | 0.00 (0.00 – 100.00) | 0.00 (0.00 – 100.00)    | 0.00 (0.00 – 100.00) | 0.00 (0.00 – 100.00)                 | 0.00 (0.00 – 100.00) |
| Others+ (n=8)                      | 44.44 (0.00 – 100.00) | 16.67 (0.00 – 83.33) | 8.33 (0.00 – 100.00)              | 0.00 (0.00 – 33.33)  | 0.00 (0.00 – 33.33)   | 0.00 (0.00 – 33.33)  | 0.00 (0.00 – 33.33)    | 0.00 (0.00 – 33.33)  | 33.33 (0.00 – 100.00)  | 0.00 (0.00 – 100.00) | 0.00 (0.00 – 100.00)        | 0.00 (0.00 – 100.00) | 0.00 (0.00 – 100.00)       | 0.00 (0.00 – 100.00) | 0.00 (0.00 – 100.00)    | 0.00 (0.00 – 100.00) | 0.00 (0.00 – 100.00)                 | 0.00 (0.00 – 100.00) |
| p value                            | 0.674                 | 0.098                | 0.647                             | 0.452                | 0.647                 | 0.452                | 0.452                  | 0.452                | 0.085                  | 0.948                | 0.368                       | 0.127                | 0.287                      | 0.287                | 0.287                   | 0.287                | 0.287                                | 0.287                |
| Diagnostic time                    |                       |                      |                                   |                      |                       |                      |                        |                      |                        |                      |                             |                      |                            |                      |                         |                      |                                      |                      |
| ≤ 3 years (n=31)                   | 33.33 (0.00 – 100.00) | 0.00 (0.00 – 100.00) | 16.67 (0.00 – 100.00)             | 0.00 (0.00 – 100.00) | 16.67 (0.00 – 100.00) | 0.00 (0.00 – 100.00) | 0.00 (0.00 – 100.00)   | 0.00 (0.00 – 100.00) | 0.00 (0.00 – 100.00)   | 0.00 (0.00 – 100.00) | 0.00 (0.00 – 100.00)        | 0.00 (0.00 – 100.00) | 0.00 (0.00 – 100.00)       | 0.00 (0.00 – 100.00) | 0.00 (0.00 – 100.00)    | 0.00 (0.00 – 100.00) | 0.00 (0.00 – 100.00)                 | 0.00 (0.00 – 100.00) |
| > 3 years (n=20)                   | 16.67 (0.00 – 100.00) | 0.00 (0.00 – 100.00) | 0.00 (0.00 – 100.00)              | 0.00 (0.00 – 100.00) | 0.00 (0.00 – 100.00)  | 0.00 (0.00 – 100.00) | 0.00 (0.00 – 100.00)   | 0.00 (0.00 – 100.00) | 0.00 (0.00 – 100.00)   | 0.00 (0.00 – 100.00) | 0.00 (0.00 – 100.00)        | 0.00 (0.00 – 100.00) | 0.00 (0.00 – 100.00)       | 0.00 (0.00 – 100.00) | 0.00 (0.00 – 100.00)    | 0.00 (0.00 – 100.00) | 0.00 (0.00 – 100.00)                 | 0.00 (0.00 – 100.00) |
| p value                            | 0.066                 | 0.164                | 0.288                             | 0.737                | 0.288                 | 0.737                | 0.737                  | 0.737                | 0.704                  | 0.961                | 0.122                       | 0.071                | 0.607                      | 0.607                | 0.607                   | 0.607                | 0.607                                | 0.607                |
| Treatment Type#                    |                       |                      |                                   |                      |                       |                      |                        |                      |                        |                      |                             |                      |                            |                      |                         |                      |                                      |                      |
| Chemotherapy (n=37)                | 22.22 (0.00 – 100.00) | 0.00 (0.00 – 100.00) | 0.00 (0.00 – 100.00)              | 0.00 (0.00 – 100.00) | 0.00 (0.00 – 100.00)  | 0.00 (0.00 – 100.00) | 0.00 (0.00 – 100.00)   | 0.00 (0.00 – 100.00) | 0.00 (0.00 – 100.00)   | 0.00 (0.00 – 100.00) | 0.00 (0.00 – 100.00)        | 0.00 (0.00 – 100.00) | 0.00 (0.00 – 100.00)       | 0.00 (0.00 – 100.00) | 0.00 (0.00 – 100.00)    | 0.00 (0.00 – 100.00) | 0.00 (0.00 – 100.00)                 | 0.00 (0.00 – 100.00) |
| Outpatient/RBCC (n=11)             | 44.44 (0.00 – 100.00) | 0.00 (0.00 – 100.00) | 33.33 (0.00 – 100.00)             | 0.00 (0.00 – 100.00) | 33.33 (0.00 – 100.00) | 0.00 (0.00 – 100.00) | 0.00 (0.00 – 100.00)   | 0.00 (0.00 – 100.00) | 33.33 (0.00 – 100.00)  | 0.00 (0.00 – 100.00) | 0.00 (0.00 – 100.00)        | 0.00 (0.00 – 100.00) | 0.00 (0.00 – 100.00)       | 0.00 (0.00 – 100.00) | 0.00 (0.00 – 100.00)    | 0.00 (0.00 – 100.00) | 0.00 (0.00 – 100.00)                 | 0.00 (0.00 – 100.00) |
| p value                            | 0.399                 | 0.810                | 0.237                             | 0.073                | 0.237                 | 0.073                | 0.073                  | 0.073                | 0.029                  | 0.323                | 0.335                       | 0.575                | 0.235                      | 0.235                | 0.235                   | 0.235                | 0.235                                | 0.235                |
| PG-SGA                             |                       |                      |                                   |                      |                       |                      |                        |                      |                        |                      |                             |                      |                            |                      |                         |                      |                                      |                      |
| Well nourished (n=33)              | 11.11 (0.00 – 88.89)  | 0.00 (0.00 – 50.00)  | 0.00 (0.00 – 100.00)              | 0.00 (0.00 – 100.00) | 0.00 (0.00 – 100.00)  | 0.00 (0.00 – 100.00) | 0.00 (0.00 – 100.00)   | 0.00 (0.00 – 100.00) | 0.00 (0.00 – 66.67)    | 0.00 (0.00 – 100.00) | 0.00 (0.00 – 100.00)        | 0.00 (0.00 – 100.00) | 0.00 (0.00 – 100.00)       | 0.00 (0.00 – 100.00) | 0.00 (0.00 – 100.00)    | 0.00 (0.00 – 100.00) | 0.00 (0.00 – 100.00)                 | 0.00 (0.00 – 100.00) |
| Mainourished (n=18)                | 44.44 (0.00 – 100.00) | 0.00 (0.00 – 100.00) | 25.00 (0.00 – 100.00)             | 0.00 (0.00 – 100.00) | 25.00 (0.00 – 100.00) | 0.00 (0.00 – 100.00) | 0.00 (0.00 – 100.00)   | 0.00 (0.00 – 100.00) | 33.33 (0.00 – 100.00)  | 0.00 (0.00 – 100.00) | 0.00 (0.00 – 100.00)        | 0.00 (0.00 – 100.00) | 0.00 (0.00 – 100.00)       | 0.00 (0.00 – 100.00) | 0.00 (0.00 – 100.00)    | 0.00 (0.00 – 100.00) | 0.00 (0.00 – 100.00)                 | 0.00 (0.00 – 100.00) |
| p value                            | 0.002                 | 0.035                | 0.057                             | 0.902                | 0.057                 | 0.902                | 0.902                  | 0.902                | 0.013                  | 0.174                | 0.250                       | 0.644                | 0.135                      | 0.135                | 0.135                   | 0.135                | 0.135                                | 0.135                |

#Mann-Whitney test; \*Kruskal Wallis. RBCC: Red blood cell concentration; PG-SGA: Patient-Generated Subjective Global Assessment; +Others: 5.9%: Hodgkin's lymphoma; 5.9%: Myeloproliferative syndrome; 3.9%: Leukemia. #N=48. Cont.= Continuation.

Table 4 presents the data on the association of the variables time of diagnosis and nutritional status – obtained through the PG-SGA – with the domains corresponding to physical, role, and cognitive functions. After adjusted linear regression analysis, the role function

domain remained associated with diagnosis time  $\leq$  3 years, indicating the latter influenced role function unfavorably. Regarding the cognitive function domain, it remained associated with malnutrition after adjusted linear regression analysis, which compromised this domain.

**Table 4:** Variables associated with domains physical function and role function of the EORTC QLQ-C30 in patients undergoing hematological cancer treatment after multivariate linear regression

| Domains            | CRUDE |                |         | ADJUSTED |                |         |
|--------------------|-------|----------------|---------|----------|----------------|---------|
|                    | Beta  | CI 95%         | p value | Beta     | IC 95%         | p value |
| Physical function  |       |                |         |          |                |         |
| Diagnostic time    |       |                |         |          |                |         |
| $\leq$ 3 years     | -13,5 | -25,86 – -1,13 | 0,033   | -9,5     | -23,32 – 4,35  | 0,174   |
| > 3 years          |       |                |         |          |                |         |
| PG-SGA             |       |                |         |          |                |         |
| Well nourished     | 13,33 | 0,66 – 26,0    | 0,4     | 10,82    | -1,63 – 23,27  | 0,087   |
| Malnourished       |       |                |         |          |                |         |
| Role function      |       |                |         |          |                |         |
| Diagnostic time    |       |                |         |          |                |         |
| $\leq$ 3 years     | -34,4 | -55,34 – -3,36 | 0,002   | -36,2    | -61,5 – -10,82 | 0,006   |
| > 3 years          |       |                |         |          |                |         |
| Cognitive function |       |                |         |          |                |         |
| PG-SGA             |       |                |         |          |                |         |
| Well nourished     | 20,87 | 7-13 – 34,62   | 0,004   | 21,23    | 6,46 – 36,0    | 0,006   |
| Malnourished       |       |                |         |          |                |         |

Linear Regression:  $p < 0,05$ . CI: Confidence Interval; PG-SGA: Patient-Generated Subjective Global Assessment. Adjusted for gender, age, race/color and type of diagnosis.

Table 5 shows the associations between nutritional status, type of treatment, and gender with the symptoms assessed by the EORTC QLQ-C30 that were associated in the initial analysis. The symptoms fatigue, nausea and vomiting, and insomnia, remained associated with

malnutrition after the adjusted linear regression analysis. This result indicates that impaired nutritional status worsens the quality of life of hematological cancer patients, based on exacerbated symptoms.

**Table 5:** Variables associated with symptoms of the EORTC QLQ-C30 in patients undergoing hematological cancer treatment after multivariate linear regression

| Symptoms            | CRUDE |               |         | ADJUSTED |               |         |
|---------------------|-------|---------------|---------|----------|---------------|---------|
|                     | Beta  | CI 95%        | p value | Beta     | IC 95%        | p value |
| EORTC QLQ-C30       |       |               |         |          |               |         |
| Fatigue             |       |               |         |          |               |         |
| PG-SGA              |       |               |         |          |               |         |
| Well nourished      | -28,8 | -36,21        | 0,002   | -28,4    | -38,97        | 0,005   |
| Malnourished        |       |               |         |          |               |         |
| Nausea and vomiting |       |               |         |          |               |         |
| PG-SGA              |       |               |         |          |               |         |
| Well nourished      | -18,5 | -26,97        | 0,006   | -18,5    | -27,3         | 0,009   |
| Malnourished        |       |               |         |          |               |         |
| Insomnia            |       |               |         |          |               |         |
| Treatment Type*     |       |               |         |          |               |         |
| Chemotherapy        | -18,3 | -39,64 – 3,09 | 0,092   | -22,1    | -45,36 – 1,22 | 0,063   |
| Outpatient/RBCC     |       |               |         |          |               |         |
| PG-SGA              |       |               |         |          |               |         |
| Well nourished      | -27,4 | -37,95        | 0,005   | -31,4    | -40,78        | 0,003   |
| Malnourished        |       |               |         |          |               |         |



**Continuation - Table 5:** Variables associated with symptoms of the EORTC QLQ-C30 in patients undergoing hematological cancer treatment after multivariate linear regression

| Symptoms       | Beta  | CRUDE         |         | Beta  | ADJUSTED      |         |
|----------------|-------|---------------|---------|-------|---------------|---------|
|                |       | CI 95%        | p value |       | IC 95%        | p value |
| Malnourished   |       |               |         |       |               |         |
| Constipation** |       |               |         |       |               |         |
| Gender         |       |               |         |       |               |         |
| Female         | -18,7 | -39,80 – 2,46 | 0,082   | -15,7 | -36,07 – 4,70 | 0,128   |
| Male           |       |               |         |       |               |         |

Linear Regression:  $p < 0,05$ . CI: Confidence Interval; PG-SGA: Patient-Generated Subjective Global Assessment. RBCC: Red blood cell concentration; Others: 5.9%: Hodgkin's lymphoma; 5.9%: Myeloproliferative syndrome; 3.9%: Leukemia; \* $n = 48$ . Adjusted for gender, age, race/color and type of diagnosis. \*\*Constipation: Adjusted for age, race/color and type of diagnosis.

## DISCUSSION

Our results showed a higher proportion of well-nourished patients with high scores on global health status and functional scales. The symptom scale and the unique items had low scores, indicating good QoL and functionality and mild symptoms. The longer time since diagnosis contributed to a better QoL, time diagnosis  $\leq 3$  years unfavorably affected physical function and functional role. Malnutrition impaired physical and cognitive functions and accentuated the symptoms of fatigue, nausea and vomiting and insomnia. Good QoL, adequate functionality and low symptoms may indicate a better prognosis, treatment success and general well-being of the patients<sup>14</sup>.

The multivariate linear regression showed an association between the time of diagnosis and the role function. The worsening of the role function in patients with shorter diagnosis time what may be related to momentary weakness, the disease itself and its treatment, as well as the patient's doubts and insecurities. However, over time, treatment can be successful, side effects are reduced, and doubts and insecurities are clarified and alleviated<sup>13</sup>, what leads to improvements and increases the patient's confidence, thus accounting for patients with longer time of diagnosis having reported better QoL in this study.

Malnutrition is a common condition in cancer patients that negatively affects quality of life, as it compromises several domains that integrate it<sup>20,21</sup>. When unidentified and untreated, it results in a poor prognosis, with a consequent increase in morbidity and mortality and reduced response and tolerance to treatment<sup>20</sup>.

A considerable impairment of cognitive function was observed among malnourished patients. According to Anderson *et al.*<sup>22</sup>, cognitive impairment is present in up to 75% of cancer patients in general, and in up to 44% of hematological cancer patients. This impairment can affect memory, visual attention and speed of information processing, limiting one's ability to perform routine tasks and worsening QoL<sup>22</sup>. Thus, an integrative and multi-professional intervention to treat this group is of marked importance, since these cognitive changes in cancer patients are subtle and may go unnoticed<sup>22</sup>.

Another domain compromised by malnutrition was physical function. Because it is a systemic inflammatory process, it is often observed in malnourished cancer

patients the loss of muscle and bone mass, resulting in a decrease in physical function.<sup>20</sup> Galindo *et al.*<sup>1</sup> identified that the impairment of physical function by malnutrition is associated with changes in appetite resulting from the worsening of nutritional status and that thus affect the other domains that make up the QOL, worsening it.

Patients with some degree of malnutrition presented worsening of fatigue, nausea and vomiting, and insomnia, even after the adjusted analyses. Fatigue is a frequent symptom in cancer patients and is reported by 50 to 90% of patients, impairing QOL and functionality, since its presence limits the patient's daily activities and well-being<sup>23</sup>.

Nausea and vomiting also had higher scores in patients with some degree of malnutrition, as shown by the results of this study. Common in cancer patients undergoing antineoplastic treatment, these symptoms can lead to loss of appetite and reduced food intake and discomfort<sup>1</sup>. Viana *et al.*<sup>24</sup> evaluated the relationship between malnutrition and the presence of symptoms of nutritional impact (SIN) in patients with different types of cancer e. These authors identified an association between these variables, highlighting the importance and need for caregivers with cancer patients during anticancer treatment. Since malnutrition directly affects the worsening of symptoms, nutritional therapy is essential for the management and reduction of associated health problems<sup>25</sup>.

Yet another symptom associated with malnutrition was insomnia. Changes in metabolism and energy balance can affect sleep, and malnutrition – as well as cancer itself – induces a systemic inflammatory process by releasing inflammatory cytokines such as IL-1, IL-6, and TNF- $\alpha$ , which affect the circadian cycle and can modulate and promote insomnia<sup>20,26,27</sup>. Salvaetti *et al.*<sup>23</sup> identified a high prevalence of insomnia in this group. These authors identified insomnia as the second most frequent symptom in cancer patients, highlighting how it can affect QoL and, therefore, how it is necessary to adopt effective strategies for its management<sup>23</sup>.

Ross *et al.*<sup>28</sup> investigated the association of insomnia and quality of life in cancer patients and concluded that women with clinical symptoms of insomnia had impaired QoL. Early intervention to prevent insomnia from becoming more persistent can be essential to improve or maintain a good QoL. Therefore, preventing, treating, and reversing malnutrition can mitigate the occurrence

of these events and, consequently, promote the patient's well-being, and should be mediated by a multidisciplinary team combined with social and family support<sup>25</sup>.

The cross-sectional characteristic of this study does not allow establishing the causal relationship between malnutrition and associated symptoms, since both are closely related. However, it demonstrates the need to recognize, investigate and treat these conditions in clinical practice.

In this context, the importance of nutritional counseling, symptom management, integrative and multi-professional intervention, periodic monitoring, and social and family support to promote nutritional and emotional support to patients is highlighted. In short, good nutritional status, adequate quality of life and functionality, and low symptoms are essential for promoting the general well-being of patients with hematologic cancer undergoing antineoplastic treatment.

The weaknesses of this study are related to the unavailability of some information on tumor staging and the chemotherapy cycle; the sample size, which can influence the results and does not allow the data to be extrapolated to other populations; the monitoring of patients on an outpatient basis, since they can be more stable; and the design of the cross-sectional study, which does not allow the identification of the causality of the facts.

As a strong points, this study presents the originality of assessing QoL in patients with hematological cancer, pointing out the implications of treatment and nutritional status on QoL, in addition to contributing to the small number of studies on this topic in this specific population. the protocols were carefully applied in a private environment after the team had been properly trained,

and when the participant felt comfortable and willing to participate. In addition, for analysis, groups were stratified by type of treatment and diagnosis.

## ■ CONCLUSION

Quality of life and functionality considered adequate were observed. Time of diagnosis and malnutrition were associated with physical and cognitive function and with the presence of fatigue, nausea and vomiting and insomnia, according to the EORTC QLQ-C30.

## Author Contributions

MSV, LPA, LFC, VRG: Developed the study protocol. MSV: Data collection, Data analysis and interpretation, Scientific writing, Final manuscript review; LPA, LFC: Data collection; GBP, TSSP, JLMR: Data analysis and interpretation, Scientific Writing; VRG: Conception and design of the Study, Coordination of data collection, Analysis and interpretation of data, Scientific Writing, Final revision of the manuscript. All authors agree to be accountable for ensuring the integrity and accuracy of the work and approved the final manuscript.

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## Conflicts of Interest

No conflicts of interest.

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## Resumo

**Introdução:** os cânceres hematológicos são responsáveis por 9% de todos os cânceres e sua progressão e tratamento afetam diretamente a qualidade de vida (QV).

**Objetivo:** avaliar a QV e fatores associados em pacientes com câncer hematológico de acordo com o EORTC QLQ-C30.

**Método:** estudo transversal realizado de agosto de 2017 a junho de 2019. Foram incluídos adultos e idosos de ambos os sexos, com câncer hematológico, em quimioterapia oral ou venosa. O estado nutricional foi avaliado pela Avaliação Subjetiva Global Gerada pelo Paciente (PG-SGA) e a QV pelo EORTC QLQ-C30.

**Resultados:** foram avaliados 51 pacientes com idade média de  $60,0 \pm 15$  anos. Destes, 51,0% eram mulheres, 80,4% eram não brancos, 37,3% apresentavam neoplasia de células linfoides B, 60,8% tinham diagnóstico  $\leq 3$  anos, 77,1% estavam em quimioterapia e 64,7% estavam bem nutridos. As pontuações para o estado de saúde global e escalas funcionais foram altas e para sintomas e itens únicos foram baixas, indicando boa QV e funcionalidade e baixa sintomatologia. Após regressão linear multivariada, o tempo de diagnóstico  $\leq 3$  anos foi associado ao desempenho funcional ( $p < 0,05$ ) e a desnutrição foi associada à função cognitiva ( $p < 0,05$ ) e aos sintomas de fadiga, náuseas e vômitos e insônia ( $p < 0,05$ ).

**Conclusões:** foi observada qualidade de vida e funcionalidade consideradas adequadas. O tempo de diagnóstico e a desnutrição foram as variáveis que se associaram com o comprometimento da função física e cognitiva e com a presença de fadiga, náuseas e vômitos e insônia, segundo o EORTC QLQ-C30.

**Palavras-chave:** Desnutrição, câncer, avaliação nutricional, desempenho funcional, cognitivo.

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