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# Nutritional status, systemic inflammation and prognosis of patients with gastrointestinal cancer

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**Abstract**

***Introduction:*** **Systemic inflammatory response in individuals with cancer is related to a progressive reduction in total body mass, especially lean mass.**

***Objective:*** **The aim of the present study was to determine the association between nutritional status and systemic inflammatory response in patients with gastrointestinal cancer.**

***Methodology:*** **A case series study was carried out involving 30 male and female adults and elderly patients with no prior treatment sent consecutively for surgery. Nutritional status was assessed using subjective and objective methods. Inflammatory response and prognosis were assessed through the determination of C-reactive protein (CRP), the Glasgow Prognostic Score and CRP/albumin ratio.**

***Results:*** **High prevalence values were found for systemic inflammation (73%), a greater risk of infectious and/or inflammatory complication (43%) and worse prognosis (50%). The percentage of weight loss was correlated with serum CRP ($r = 0.38$; $p < 0.05$) and the CRP/albumin ratio ($r = 0.44$; $p < 0.05$). Inflammation markers and prognosis were negatively correlated with serum albumin ($r = -0.50$; $p < 0.05$), body mass index ($r = -0.39$; $p < 0.05$) and total lymphocyte count ($r = -0.37$; $p < 0.05$). Patients with weight loss and malnourishment had significantly higher serum CRP and CRP/albumin ratio values as well as lower serum albumin levels in comparison to those without weight loss and in well-nourished.**

***Conclusion:*** **Nutritional status is related to inflammation markers and prognosis in patients with gastrointestinal cancer. The diagnosis and attenuation of systemic inflammation should be part of the nutritional care of these patients.**

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Key words: *Cancer. Gastrointestinal tract. Malnutrition. Inflammation. C-reactive protein.*

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**EL ESTADO NUTRICIONAL, LA INFLAMACIÓN SISTÉMICA Y EL PRONÓSTICO DE LOS PACIENTES CON CÁNCER GASTROINTESTINAL**

**Resumen**

***Introducción:*** **En los individuos con cáncer, la respuesta inflamatoria sistémica es relacionada a la progresiva disminución de la masa corpórea total, principalmente de la masa magra.**

***Objetivo:*** **Verificar la relación entre el estado nutricional y la actividad inflamatoria sistémica en pacientes con cáncer del trato gastrointestinal.**

***Metodología:*** **estudio tipo serie de casos, envolviendo 30 pacientes adultos y ancianos de ambos sexos, sin tratamiento anterior, enviados consecutivamente para cirugía. El estado nutricional fue evaluado por métodos subjetivo y objetivo, y la actividad inflamatoria y el pronóstico por medio de proteína C-reactiva (PCR), Puntuación Pronóstico de Glasgow (GPS) y Relación Proteína C-reactiva/albumina.**

***Resultados:*** **Se verificó elevada prevalencia de pacientes con inflamación sistémica (73%), mayor riesgo de complicación infecciosa y/o inflamatoria (43%) y peor pronóstico (50%). El porcentual de pérdida de peso se correlacionó con la PCR seria ($r = 0,38$; $p < 0,05$) y la relación PCR/albumina ($r = 0,44$; $p < 0,05$). Hubo correlación negativa de la albumina sérica ($r = -0,50$; $p < 0,05$), del Índice de Masa Corporal ($r = -0,39$; $p < 0,05$) y del Cómputo Total de Linfocitos ($r = -0,37$; $p < 0,05$) con los marcadores de inflamación y pronóstico. Los pacientes con pérdida de peso y desnutridos presentaban valores significativamente mayores de PCR sérica y relación PCR/albumina, y menores de albumina sérica cuando comparados con aquellos sin pérdida de peso y eutróficos.**

***Conclusión:*** **El estado nutricional es relacionado con los marcadores de inflamación y pronóstico. Se sugiere que el diagnóstico y la atenuación de la inflamación sistémica sean parte del cuidado nutricional de estos pacientes.**

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Palabras clave: *Trato gastrointestinal. Desnutrición. Inflamación. Proteína C-reactiva.*

## Abbreviations

TNF-α = Tumor necrosis factor-alpha.
IFN-γ = Interferon γ.
IL-1 = Interleukin-1.
IL-6 = Interleukin-6.
IL-8 = Interleukin-8.
PG-SGA = Patient-generated subjective global assessment.
W = Weight.
H = Height.
BMI = Body mass index.
CRP = C-reactive protein.
%WL = Percentage of weight loss.
TSF = Triceps skinfold.
AC = Arm circumference.
AMC = Arm muscle circumference.
GPSm = Modified Glasgow Prognostic Score.
TNM = T (extension of primary tumor); N (metastasis in regional lymph node); M (distant metastasis).
TLC = Total lymphocyte count.
Hb = Hemoglobin.
Ht = Hematocrit.

## Introduction

Estimates indicate a high occurrence of gastrointestinal cancer in Brazil in 2010/2011, represented mainly by 28 thousand cases of colon/rectal cancer and 21 thousand cases of stomach cancer.[1] Diet is a major factor in the etiology of cancer and is responsible for approximately 70% of cases of the disease in the digestive tract.[2] The dietary risk factors for carcinogenesis include a high consumption of animal fat, salt, alcohol, smoked foods, canned foods, processed meat and food with food coloring as well as a low intake of fruit, vegetables and cereals.[1,3]

The presence of a malignant tumor can lead to an increase in inflammatory mediators, such as the cytokines interleukin-1 (IL-1), interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α) and interferon (IFN-γ). The prolonged or excessive secretion of these cytokines can have diverse effects related to anorexia and cachexia (wasting syndrome), such as the depletion of fat stocks, an increase in protein degradation in skeletal muscle and an increase in the synthesis of acute-phase proteins, such as C-reactive protein (CRP).[4] Thus, a number of researchers have sought to understand the association between the inflammatory state of individuals with cancer and the development of anorexia and cachexia.[5,6,7,8]

The most common measure of systemic inflammatory response in patients with cancer is the high concentration of serum CRP, which is currently included in recent definitions of cachexia stemming from cancer. Another manner to assess the inflammatory state is through the use of scales, such as the Glasgow Prognostic Score (GPS), which includes two serum indicators: CRP and albumin.[9] This scale is capable of identifying patients who will likely develop cachexia and have a reduced response to cancer treatment and lower survival rate.[10] The CRP/albumin ratio is another commonly employed measure and constitutes an alternative for the simplification of the original formula of the Prognostic Inflammatory and Nutritional Index.[11]

The aim of the present study was to determine the association between nutritional status and systemic inflammatory response in patients with gastrointestinal cancer.

## Methods

### *Patients*

A case-series, cross-sectional study was carried out involving 30 patients hospitalized at the Surgical Clinic of the Barão de Lucena Hospital in the city of Recife (Brazil) with a diagnosis of gastrointestinal cancer and indication for surgical treatment between April and July 2010. The patients were studied consecutively within 72 hours following admission.

The following were the inclusion criteria: age 18 years or older; either sex; any race; diagnosis of gastrointestinal cancer based on histological analysis (carcinoma and adenocarcinoma), including mouth, esophagus, stomach, pancreas, duodenum, liver, colon or rectum; any clinical stage of the disease (I to IV) for the classification of malignant tumors (Tumor, Nodes and Metastasis (TNM) of the Union for International Cancer Control).[12] The clinical information was provided by the head surgeon. The exclusion criteria were a previous history of treatment (chemotherapy, radiotherapy or surgery), presence of a inflammatory or infectious acute or chronic process, cold (influenza), and concomitant presence of other diseases that may affect nutritional status and/or systemic inflammatory response, such as diabetes mellitus, chronic kidney failure, liver disease, heart disease, lung disease and trauma.

The study received prior approval from the Human Research Ethics Committee of Agamenon Magalhães Hospital (Recife, Brazil) under process nº. 16/2010, in compliance with Resolution 196/96 on Research Involving Human Subjects of the National Health Council of the Brazilian Ministry of Health. All patients participated voluntarily and signed terms of informed consent.

### *Assessment of nutritional status*

The nutritional assessment was performed using subjective and objective techniques.

For the subjective method, the patient-generated subjective global assessment (PG-SGA) proposed by Ottery et al. was used.[13] Nutritional status was classified as Grade A (well nourished), Grade B (moderate

malnutrition or suspicion of malnutrition) and Grade C (severe malnutrition). As recommended by Detsky et al.,[14] the highest judgment was placed on the following variables: weight loss, reduced dietary intake, loss of subcutaneous adipose tissue and loss of muscle mass. For analysis purposes, patients classified as Grades B and C by the PG-SGA were considered malnourished.

Anthropometric, laboratory and dietary indicators of nutritional status constituted the objective measures.

The anthropometric evaluation involved the determination of current weight (W) and height (H) on an anthropometric scale (FilizolaTM); arm circumference (AC) with a non-stretchable cellulose tape on the midpoint of the arm between the acromion and olecranon; and triceps skinfold (TSF) with an appropriate clinical adipometer (Cescorf®). From these data, derived indexes were calculated: percentage of weight loss (%WL) in relation to habitual weight (habitual W– current W x 100/habitual W), body mass index (BMI = $W/H^2$) and arm muscle circumference (AMC = AC– [0.314 x TSF]). %WL in the previous six months was categorized as significant (5 to 10%) and severe (> 10%).[15] The cutoff points for BMI ($kg/m^2$) determined by the World Health Organization were used for the classification of the adults patients: < 18.5 (underweight), 18.5 to 24.9 (ideal range), 25 to 29.9 (overweight) and ≥ 30 (obesity).[16] The cutoff points determined by the Pan American Health Organization were used for the classification the elderly patients (aged 60 years or older): < 23 (underweight), 23 to 28 (ideal range), and ≥ 28 (overweight).[17] For the other anthropometric indicators (AC, AMC and TSF), adequacy percentages were calculated to classify nutritional status. Malnutrition was classified as severe (< 70%), moderate (≥ 70 and < 80%) and mild (≥ 80 and < 90%). Patients with values ≥ 90 and < 110% were considered well nourished. Excess weight demonstrated by the AC and TSF was subdivided into overweight (≥ 110 and < 120%) and obesity (≥ 120%).[15]

Blood samples (20 mL) were collected from a peripheral vein with a single puncture in the morning following rest and eight hours of fasting for the hematological and biochemical exams, following the standardized procedures of the Clinical Analysis Laboratory of the Barão de Lucena Hospital. The following variables were studied: hemoglobin (Hb), hematocrit (Ht), leukocytes, total lymphocyte count (TLC), albumin, glucose and CRP. Hb, Ht, leukocytes and TLC were analyzed using an automated electronic cell counter (SYSMEX XT 2000, Roche®) and reviewed through optical microscopy on a blood swab. The biochemical variables were determined and analyzed using an automated biochemical analyzer (Cobas Integra 400, Roche®): albumin (bromocresol green colorimetric method, Albumin Plus, Roche®) and fasting glucose (hexokinase/glucose-6-phosphate dehydrogenase, Glucose HK, Roche®).

The normal values used for Hb (g/dL) were 13.5 to 18.0 for men and 12.0 to 16.0 for women; and the values for Ht (%) were 40 to 54 for men and 38 to 47 for women.[18] The normal values for leukocytes were 4,500 to 11,000 mm.[18] The TLC was determined by leukograms using the percentage of lymphocytes in relation to the TLC (cells/$mm^3$) (TLC = lymphocytes x leukocytes/100) and the patients were classified as having normal nutritional status (> 2,000), mild malnutrition (1,200 to 2,000), moderate malnutrition (800 to 1,199) and severe malnutrition (< 800). The albumin results (g/dL) were classified as normal (> 3.5), mild depletion (3.0 to 3.5), moderate depletion (2.4 to 2.9) and severe depletion (< 2.4).[18] The reference values adopted for glycemia (mg/dL) were < 100 (normal), 100 to 125 (glucose intolerance) and ≥ 126 (hyperglicemia or diabetes).[19]

The 24-hour recall method was used for the assessment of recent calorie and protein intake.[20] The patient was interviewed by the researcher upon admission to hospital for the record of all foods and beverages consumed in the previous 24 hours. The data were transcribed in household measures and subsequently converted into portion or food weight. The dietary calculations were performed using the Avanutri program (version 3.1.1).

Individual nutritional needs for calories and protein were calculated based on the recommendations for adult cancer patients in the preoperative period established by the National Oncologic Nutrition Consensus of the Brazilian National Cancer Institute.[21] Caloric need was defined based on the result of the PG-SGA. The aim was to maintain weight (30 kcal/kg/day) among patients classified as Grade A; the aim was weight gain (35 kcal/kg/day) for those classified as Grade B; and repletion was considered (45 kcal/kg/day) for those classified as Grade C. With regard to individual protein needs, the recommendation of the National Cancer Institute considers the degree of metabolic stress,[21] which in the present study is classified based on the serum CRP value. A protein need of 1.2 g/kg/day was considered for patients with CRP up to 0.5 mg/dL (absence of metabolic stress); a protein need of 1.5 g/kg/day was considered for those with CRP between 0.5 and 1.0 mg/dL (moderate metabolic stress); and a protein need of 2.0 g/kg/day was considered for those with values greater than 1.0 mg/dL (indicative of systemic inflammatory response syndrome).

### *Assessment of systemic inflammatory activity and prognostic indexes*

Inflammatory response was assessed based on serum CRP values, which were determined and analyzed by an automated biochemical analyzer using the immunoturbidimetric assay (CRP latex HS, Roche®).[22] The reference value adopted for normality was < 0.5 mg/dL, whereas 0.5 to 1.0 mg/dL was considered indicative of a risk of inflammation[10] and values above 1.0 mg/dL indicated systemic inflammatory response syndrome.[23,24,25]

**Table I**
*Epidemiological and clinical characteristics of patients with gastrointestinal cancer at Barão de Lucena Hospital, Recife, Brazil, 2010*[1]

| *Variables* | *Results* | |
|---|---|---|
| | *N* | *%* |
| *Age (years)* | | |
| < 60 | 11 | 37 |
| ≥ 60 | 19 | 63 |
| *Gender* | | |
| Female | 15 | 50 |
| Male | 15 | 50 |
| *Location of tumor* | | |
| Colon | 09 | 30 |
| Rectum | 07 | 24 |
| Stomach | 06 | 20 |
| Pancreas | 03 | 10 |
| Colon/Rectum | 02 | 7 |
| Bile ducts | 01 | 3 |
| Esophagus | 01 | 3 |
| Small intestine | 01 | 3 |
| *Clinical stage** | | |
| I/II | 12 | 40 |
| III/IV | 18 | 60 |

[1]n = 30; % = absolute percentage in relation to total number of patients.
*Based on TNM system of Union for International Cancer Control (2010).

Prognosis was determined based on the modified Glasgow Prognostic Score (GPSm) and CRP/albumin ratio.[9,11] The GPSm uses two serum indicators (CRP and albumin) and its classification is determined based on scores, as follows: patients with high CRP (≥ 1.0 mg/dL) and hypoalbuminemia (< 3.5 g/dL) received 2 points; those with only high serum CRP received 1 point; and those with neither abnormality received 0 points.[9] Based on the CRP/albumin ratio, the patients were classified as having no risk (< 0.4), low risk (0.4 to 1.2), moderate risk (1.2 to 2.0) or high risk (< 2) of infectious and inflammatory complications.[26]

*Statistical analysis*

Qualitative variables were expressed as percentage values and quantitative variables were expressed as either mean and standard deviation values (normal distribution) or median values and 25th and 75th percentiles (non-parametric distribution). Significant differences between groups were determined using the Student's t-test and Mann-Whitney test for data with parametric and non-parametric distribution, respectively. Differences in mean values between groups were determined using one-way ANOVA and the Holm-Sidak test for parametric data and the Kruskal-Wallis test and Dunn's test for non-parametric data. Spearman's correlation coefficients were calculated for the determination of correlations between variables. The analyses were performed using the Sigma Stat for Windows, version 3.5 (SPSS, Chicago, IL, USA), with the level of significance set at 5%.

## Results

The sample was made up of 15 men (50%) and 15 women (50%). Age ranged from 27 to 91 years (mean: 61 years). Colon cancer was the most frequent (30%), followed by cancer of the rectum (23%) and stomach (20%). The majority were in the advanced phase of the disease (clinical stages III and IV) (60%) (table I) and had been diagnosed recently (time elapsed since diagnosis < 6 months) (86.6%). The mortality rate was 16.6%.

Malnutrition was found in a high percentage of patients. The subjective method (PG-SGA) detected a largest number of malnourished patients (83%) in comparison to the objective method: TSF (80%), %WL (70%), AC (67%), AMC (57%) and BMI (40%). By anthropometrics, the depletion of subcutaneous adipose tissue (diagnosed using the TSF) was the most prevalent. BMI was the indicator that least detected malnutrition. Severe weight loss (> 10%) in the previous six months was found in 20 (67%) patients.

Seventy percent of patients were immunocompromised (TLC less than 2,000/mm$^3$), with moderate to severe lymphocyte depletion found in 33%. Malnourished patients (based on the PG-SGA) had lower TLC values in comparison to well-nourished patients (1,438 ± 656 *vs.* 2,307 ± 765; p = 0.014).

Regarding the hematological variables, mean Hb (11.19 ± 2.44 for men and 11.59 ± 1.64 for women) and Ht (34.92 ± 6.73 for men and 36.01 ± 5.54 for women) were within the normal range for the women and slightly below normal among the men in comparison to the reference values. However, high frequencies of reduced Hb (67%) and Ht (70%) were found, suggesting anemia. Hypoalbuminemia was found in 53% and white blood vessels above the reference value were found in 37% of the patients.

Median (25th and 75th percentile) calorie intake was 1,547.9 (1,137.1-1,851.6) kcal/day and mean (± standard deviation) protein intake was 72.9 ± 36.4 g/day. In comparison with the estimated calorie (2,093.8 ± 336.8) and protein (101.7 ± 25.8) needs, dietary intake was significantly reduced (p < 0.001).

High prevalence values were found for systemic inflammation (73%), represented by altered serum CRP values; a greater risk of complications (43%), represented by the CRP/albumin ratio; and a poor prognosis (50%), based on the GPSm.

**Table II**
*Correlations between inflammatory markers and prognosis according to anthropometric, laboratory and dietary variables in patients with gastrointestinal cancer at Barão de Lucena Hospital, Recife, Brazil, 2010*[1]

| *Indicators* | *Serum CRP* | *CRP/Albumin ratio* |
|---|---|---|
| BMI | -0.390* | -0.390* |
| AC | -0.323 | -0.320 |
| TSF | -0.219 | -0.185 |
| AMC | -0.186 | -0.213 |
| %WL | 0.377* | 0.442* |
| Serum albumin | -0.502* | -0.629* |
| TLC | -0.366* | -0.353* |
| Calorie intake | -0.0585 | -0.114 |
| Protein intake | -0.236 | -0.230 |

[1]n = 30; BMI = Body mass index; AC = Arm circumference; TSF = Triceps skinfold; AMC = Arm muscle circumference; %WL = Percentage of weight loss; CRP = C-reactive protein; TLC = Total lymphocyte count; Spearman's correlation coefficients for pairs of variables; *p < 0.05.

For the correlations of serum CRP and the CRP/albumin ratio in the univariate analysis, a significant positive correlation was found with %WL, whereas significant negative were found with albumin, BMI and TLC (table II).

Patients with weight loss and malnutrition based on the PG-SGA had significantly higher serum CRP and CRP/albumin values as well as lower serum albumin in comparison to those who were well-nourished and without weight loss (table III). The same was not observed when BMI was compared with serum CRP (p = 0.496), the CRP/albumin ratio (p = 0.558) and serum albumin (p = 0.268).

Patients with advanced cancer had significantly lower BMI, AC, AMC and serum albumin values and higher %WL and CRP/albumin ratio values in comparison to those with cancer in an early stage. However, serum CRP and dietary intake data were not significantly different between the different stages of cancer (table IV).

## Discussion

Individuals with cancer develop anorexia-cachexia syndrome during the progression of the disease, especially those with advanced tumors in the upper gastrointestinal tract.[27] The subjective assessment method has been used as a nutritional screening tool at admission to hospital to identify malnourished individuals and those at risk of malnutrition, who are candidates for nutritional therapy and monitoring.[21,28]

In the present study, the prevalence of compromised nutritional status varied with the assessment method employed. The PG-SGA detected the highest prevalent nutritional deficit in relation to the anthropometric indicators. Subcutaneous adipose tissue depletion (determined by the TSF) had the second prevalence value, followed by percentage of weight loss and muscle mass depletion. The BMI indicated the lowest prevalence of compromised nutritional status, which corroborates findings reported in previous studies,[29,30,31] thereby limiting the use of this isolated indicator for nutritional assessments even among patients with cancer. Thus, 25 patients in the present study were indicated for nutritional therapy based on the subjective nutritional screening assessment.

Few studies have assessed systemic inflammation leading to an increase in inflammatory cytokines and serum CRP in patients with gastrointestinal cancer. Chronic inflammatory disease, such as cancer, can produce a persistent increase in the serum concentration of CRP. Among the patients studied, 73% had high serum CRP levels as well as high GPS values. Studying patients with esophagus and stomach cancer, Deans et al.[8] found an increase in this serum protein in 83%. In other studies, 24% of patients with colon-rectal cancer had altered CRP values,[9] whereas this figure was 10% among patients with head and neck cancer.[32] In a sample of 24,062 patients with cancer, Proctor et al.[28] found that the systemic inflammatory response —evidenced by higher GPS values (scores of 1 or 2)— varied with the

**Table III**
*Acute-phase proteins and prognostic index according to altered body weight and nutritional status in patients with gastrointestinal cancer at Barão de Lucena Hospital, Recife, Brazil, 2010*[1]

| *Variables* | *% of weight loss* | | *p* | *PG-SGA* | | *p* |
|---|---|---|---|---|---|---|
| | *Present (n = 21)* | *Absent (n = 9)* | | *A (n = 5)* | *B + C (n = 25)* | |
| CRP (mg/dL) | 5.32(1.79-10.99) | 1.17(0.46-2.12) | 0.040* | 0.62(0.21-1.51) | 5.26(1.79-10.99) | 0.018* |
| Albumin (g/dL) | 3.18 ± 0.58 | 4.01 ± 0.58 | 0.001* | 4.08 ± 0.78 | 3.30 ± 0.60 | 0.017* |
| CRP/Alb ratio | 1.78(0.65-4.04) | 0.37(0.11-0.55) | 0.016* | 0.15(0.05-0.43) | 1.72(0.50-4.04) | 0.014* |

[1]n = 30: data expressed as mean and standard deviation and median with 25th and 75th percentiles; Mann-Whitney test used for non-parametric data; Student's t-test used for parametric data; *p < 0.05; PG-SGA = Patient-generated subjective global assessment; CRP = C-reactive protein; Alb = Albumin.

**Table IV**
*Anthropometric, dietary and laboratory indicators, inflammatory markers and prognosis according to clinical stage of disease in patients with gastrointestinal cancer at Barão de Lucena Hospital, Recife, Brazil, 2010*[1]

| *Variables* | *Clinical stage* | | *p* |
|---|---|---|---|
| | *Early (I and II) (n = 12)* | *Advanced (III and IV) (n = 18)* | |
| *Anthropometric* | | | |
| BMI | 24.30 ± 5.04 | 20.98 ± 3.72 | 0.047* |
| %WL | 6.50 ± 11.28 | 20.23 ± 10.68 | 0.002* |
| TSF | 14.92 ± 8.45 | 10.89 ± 6.58 | 0.154 |
| AC | 28.33 ± 4.11 | 25.01 ± 3.46 | 0.024* |
| AMC | 23.65 ± 2.62 | 21.59 ± 2.47 | 0.038* |
| *Dietary* | | | |
| Calories | 1,535.29 (1,165.95-2,245.34) | 1,547.94 (1,086.16-1,698.00) | 0.446 |
| Protein | 84.81 (54.23-126.76) | 64.31 (44.70-79.50) | 0.099 |
| *Laboratory* | | | |
| Serum albumin (g/dL) | 3.915 ± 0.633 | 3.107 ± 0.525 | < 0.001* |
| *Inflammatory markers* | | | |
| Serum CRP (mg/dL) | 0.97 (0.58-6.20) | 5.29 (1.98-10.30) | 0.079 |
| CRP/Alb ratio | 0.28 (0.14-1.97) | 1.75 (0.66-4.10) | 0.038* |

[1]n = 30: data expressed as mean and standard deviation and median with 25th and 75th percentiles; one-way ANOVA followed by Holm-Sidak test used for parametric data; Kruskal-Wallis test or Kruskal-Wallis followed by Dunn's test used for non-parametric data; *p < 0.05; BMI = Body mass index; %WL = Percentage of weight loss; TSF = Triceps skinfold; AC = Arm circumference; AMC = Arm muscle circumference; CRP = C-reactive protein; Alb = Albumin.

type of tumor; the proportion of patients with systemic inflammation was higher for hepatobiliary (68%), lung (64%), stomach (55%), head and neck (54%) and pancreatic (52%) cancer. Beside the type of tumor, it has been suggested that the size of the primary tumor is associated with high concentrations of serum CRP, as found in patients with operable colon-rectal cancer.[33]

Weight loss is the nutritional indicator most related to serum CRP. Studying patients with esophagus and stomach cancer, Deans et al.[8] found the following variables to be determinant of weight loss: dietary intake, high serum CRP concentration and stage of the disease. The attenuation of systemic inflammatory response has been studied as a way to improve nutritional status. Supplementation with omega-3 fatty acids may help stabilize weight in cancer patients with oral dietary intake who exhibit intentional, progressive weight loss.[34]

In the present study, two anthropometric indicators (BMI and %WL) were related to both systemic inflammation (serum CRP) and an advanced stage of the disease, whereas muscle mass (determined by AC and AMC) was different only in advanced stages. The advanced stage of the disease can act as an indirect measure of the tumor load, increasing the metabolic demands of the patient, but may also result in an increase in the production and release of biological mediators, such as pro-inflammatory cytokines and other tumor-derived products, which may contribute toward the metabolic changes associated with anorexia and cachexia.[33] In the present sample, patients in advanced stages of the disease had higher CRP/ albumin ratio values, suggesting a greater risk of complications stemming from inflammatory stress, as well as higher serum CRP values, although the difference in this variable did not achieve statistical significance. Similarly to what was found with the anthropometric indicators (BMI and %WL), the subjective method (PG-SGA) revealed higher serum CRP values in malnourished individuals in comparison to those who were well-nourished. Therefore, a poorer nutritional status and advanced stage of the disease were related to the systemic inflammatory response.

A possible limitation of the present study was not having confirmed the results of serum CRP among the patients with increased values in the preoperative period through the repetition of the laboratory exam. The confirmation of the results after two or three weeks is recommended, as serum CRP concentrations rise in response to infection, surgery, trauma and acute inflammatory events. However, is likely that these factors did not influence the results, as the patients studied were in favorable clinical conditions to undergo surgery the day following the collection of the blood sample for the quantification of CRP.

Reduced dietary intake stemming from anorexia may be a response through the intermediation of the action of TNF-α, IL-1, IL-6 and IFN-γ.[5,6,7] However, no

associations were found in the present sample between dietary intake data and inflammation or prognosis. A number of gastrointestinal symptoms can affect dietary intake, which is often diminished in the presence of cancer. In the present study, the following symptoms were reported by the patients in the PG-SGA: pain (38%), vomiting (28%), nausea (25%) and diarrhea (22%).

Immune system deficiency in cancer is multifactor due to the tumor itself, cachexia, poor dietary intake, surgical trauma and treatment. Malnutrition is a factor that can affect the TLC, thereby compromising immunological status. However, the lymphocyte count can increase in the presence of bacterial infection. Based on TLC values, 21 of the patients in the present study exhibited immune deficiency, which was related to both nutritional status and inflammatory response (an increase in serum CRP). Studying 287 patients with colon-rectal cancer, Roxburgh et al.[35] found that the systemic inflammatory response (determined by an increase in the GPS value) was associated with a reduced TLC as well as increased white blood cell and neutrophil counts. Thus, the presence of systemic inflammation is among the factors related to immunological alterations. In the present study, leukocytosis was found in 11 patients, likely as the result of the cancer itself, as the presence of infection is a contraindication for the elective surgical procedure.

In conclusion, the findings of the present study demonstrate that patients with gastrointestinal cancer have high prevalence of malnutrition, systemic inflammation and poor prognosis. Nutritional status is associated with systemic inflammatory response and the advanced stages of the disease. Therefore, the implantation of a nutritional protocol is suggested for patients with gastrointestinal cancer, with an early assessment of nutritional status and systemic inflammatory response (serum CRP).

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