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Relationship between nutritional status and the Glasgow Prognostic Score in patients with colorectal cancer

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Objective: The association between nutritional status and inflammation was assessed in patients with colorectal cancer and to verify their association with complications during anticancer treatment. The agreement between the Subjective Global Assessment (SGA) and different nutritional assessment methods was also evaluated.
Methods: A cross-sectional, prospective, and descriptive study was performed. The nutritional status was defined by the SGA and the severity of inflammation was defined by the Glasgow Prognostic Score (GPS). The complications were classified using the Common Toxicity Criteria, version 3. Anthropometric measurements such as body mass index, triceps skinfold, midarm circumference, midarm muscle area, and adductor pollicis muscle thickness were also performed, as were handgrip strength and phase angle. The chi-square test, Fisher exact test, Spearman correlation coefficient, independent *t* test, analysis of variance, Gabriel test, and κ index were used for the statistical analysis. $P < 0.05$ was considered statistically significant.
Results: Seventy patients with colorectal cancer (60.4 ± 14.3 y old) were included. The nutritional status according to the SGA was associated with the GPS ($P < 0.05$), but the SGA and GPS were not related to the presence of complications. When comparing the different nutritional assessment methods with the SGA, there were statistically significant differences.
Conclusion: Malnutrition is highly prevalent in patients with colorectal cancer. The nutritional status was associated with the GPS.

Introduction

The overall impact of cancer has more than doubled in 30 y according to the most recent report by the International Agency for Research on Cancer of the World Health Organization [1]. Colorectal cancer progresses with metabolic and nutritional complications [2,3], which are associated with a decreased response to treatment. Therefore, it is important to develop effective strategies and practices for early nutritional diagnosis. Within this perspective, the routine assessment of patient nutrition is extremely necessary for an early intervention to result in a more favorable clinical outcome and improved quality of life for these patients.

Patients with cancer are in a state of chronic inflammation. The Glasgow Prognostic Score (GPS) has been used to classify the degree of inflammation based on the levels of C-reactive protein (CRP) and albumin [4]. The GPS may be a potentially useful method for the diagnosis of nutritional status because inflammation is one of the factors that contribute to the development of cachexia, which worsens nutritional status. Moreover, the presence of inflammation and weight loss has been associated with the development of complications during cancer treatment.

There is controversy about the best technique for the characterization of nutritional status. Several nutritional assessment tools, which are essentially objective, have been used in clinical practice, with advantages and disadvantages. Anthropometric indicators, such as the body mass index (BMI), triceps skinfold (TSF), midarm circumference (MAC), and midarm muscle area (AMA) are routinely used in clinical practice because of the cost benefit [5]. These methods are inexpensive and easily performed [6]. The adductor pollicis muscle thickness (APMT) is a relatively new anthropometric parameter that has been used to assess the muscle compartment and, indirectly, nutritional status.

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Bioelectrical impedance analysis also has been used to assess body composition in patients with cancer [7]. Bioelectrical impedance analysis can be used to determine the phase angle (PA), which represents the electrical current stored by cell membranes [8]. Lower PA values suggest cell death or decreased cellular integrity, whereas higher values indicate larger amounts of intact cell membranes and a better nutritional status. The handgrip strength (HGS), a functional test of the skeletal muscle, has received increased attention from clinicians and researchers in recent years because functional indicators are often related to nutritional status. They are of particular importance because they are associated with the loss of functional capacity and clinical complications [9]. The agreement between all these methods and the Subjective Global Assessment (SGA), considered in this report as the gold standard for nutritional assessment, should be further investigated because the discussed methods are routinely used by many professionals but are not necessarily ideal for use in patients with cancer.

Thus, the present study evaluated the association between nutritional status and the GPS and their association with complications during anticancer treatment. Another objective was to assess the agreement between nutritional assessment methods and the SGA.

Materials and methods

The present study was a cross-sectional, prospective, and descriptive study performed in the Hospital Borges da Costa/Hospital das Clínicas, Universidade Federal de Minas Gerais, Minas Gerais, Brazil. The research was reviewed and approved by the ethics committee on research at the Universidade Federal de Minas Gerais (ETIC 0601.0.203.000-0). Patients who were diagnosed with cancer of the colon and rectum and were older than 18 y were invited to participate in the study. The exclusion criteria were the presence of infection and non-cancer inflammatory diseases, the presence of kidney and liver diseases, and the use of diuretics. All patients provided informed consent.

A standardized questionnaire was used to collect the data, including name, age, sex, type of treatment, cancer staging, assessment of nutritional status by various methods, complications, and death. Data were collected before starting chemotherapy or radiotherapy treatment. Complications were classified using the Common Toxicity Criteria, version 3 [10], and the following complications were considered: hematologic toxicity (platelets and leukocytes, grade 2), gastrointestinal toxicity (nausea, vomiting, diarrhea, and mucositis, grade 2), and infections (documented infection, grade 2; febrile neutropenia, grade 3). Information regarding adverse events was collected from the patients' records. Complications were assessed for 3 mo after the first interview.

Anthropometric measurements, including BMI, TSF, MAC, AMA, and APMT, were performed by trained dietitians. Weight was measured on a mechanical scale (Filizola, São Paulo, Brazil), with the patient standing in the center of the platform wearing light clothing and no shoes. Height was determined using a stadiometer fixed to the scale, on which the patient stood barefoot, with the patient's back to the scale, standing straight, and eyes facing forward. Weight and height were used to calculate the BMI (weight in kilograms/height in meters squared). The patients were considered nourished if the BMI was greater than 18.5 kg/m^2 in adults and greater than 22 kg/m^2 in the elderly.

To obtain the MAC, the patient's arm was flexed toward the chest, forming an angle of 90°. The midpoint between the acromion and the olecranon was identified and marked. Afterward, the patient's arm was extended along the body with the palm facing the thigh. On the marked point, a flexible tape of 2.00 m, adjusted to avoid compression of the skin, was used around the patient's arm. The TSF was obtained at the same set point as for the MAC, using the Lange skinfold caliper (Santa Cruz, California, USA). The MAC and TSF were classified according to the method of Frisancho [11]. Thus, nourished patients were those in the 15th percentile. The AMA was also classified according to the method of Frisancho [12], and nourished patients had a percentile higher than 10. The APMT was measured with the subject in a seated position, the dominant hand on the ipsilateral knee, and an elbow angle of about 90°. The Lange caliper was used to clamp the adductor muscle at the apex of an imaginary angle formed by the extension of the thumb and the forefinger. The APMT was classified according to the values proposed by Gonzalez et al. [13], using the highest value of three measurements.

To measure bioimpedance, the Quantum X model (RJL Systems, Michigan, USA) was used. The measurements were performed with the patient lying supine with the arms and legs extended about 45° from the body after at least 4 h of fasting. The resistance and reactance provided by the device were used to calculate the percentage of body fat, lean mass, and the PA. The fat-free mass and total body fat were calculated using the equation developed by Chumlea et al. [14] validated in the Third National Health and Nutrition Examination Survey. The PA was calculated as the arc tangent of the ratio of reactance to resistance in degrees. The PA was converted into a standardized PA according to Barbosa-Silva et al. [15] who used Brazilian population to develop this standard.

The HGS was tested using the Dynamometer Plus (Jamar, South RD Hilton, South Australia, Australia), with the patient sitting with the arms supported. The average of three measurements was taken according to the method of Budziareck et al. [16].

Patients were classified according to the SGA as nourished (SGA A), suspected malnutrition or moderately malnourished (SGA B), or severely malnourished (SGA C) [17]. In relation to the GPS, patients who had increased CRP levels (>10 mg/L) and hypoalbuminemia (<3.5 mg/L) were allocated as GPS 2. Patients who had increased CRP levels were allocated as GPS 1, and those with normal CRP with or without hypoalbuminemia were allocated as GPS 0 [18].

Statistical analysis

SPSS 19.0 (SPSS, Inc., Chicago, IL, USA) was used for statistical analysis. $P < 0.05$ was considered statistically significant. The chi-square test was used to assess the association between the SGA classes and the GPS. The other associations were evaluated using the Fisher exact test. The Spearman correlation coefficient was used to verify the correlation between albumin and CRP. The independent *t* test was used to verify the association between age and sex. Analysis of variance was used to compare the parameters of nutritional assessment among the SGA classes. The Gabriel test was used for multiple comparisons. The κ index was used to assess the agreement between the results of the different nutritional assessment methods and the SGA.

Results

Seventy patients (31 men and 39 women) were evaluated. The general population data, divided by sex, are presented in Table 1.

The overall prevalence of malnutrition (SGA B and C) in this population was 70%, and 45.7% of patients had severe malnutrition (SGA C). The percentage of weight loss in the previous 6 mo, information also assessed by the SGA, showed that a significant number of patients (44.9%) presented with severe weight loss. Nine patients (13%) had not lost any weight. Sex ($P > 0.05$, Fisher test) and age (chi-square = 2.25, $P > 0.05$) were not associated with nutritional status.

Inflammation measured by the GPS showed that 8.1% of patients had a score of 2 and 27.4% a score of 1. Most patients (64.5%) were classified as score 0. The SGA-to-GPS ratio was evaluated for 62 patients (Fig. 1). Data from eight patients were

Table 1
General data of the population by gender evaluated at Hospital Borges da Costa from April 2010 to September 2011; Belo Horizonte, 2012

Variable	Men (44.3%)	Women (55.7%)	P
Age (y), mean ± SD	60.1 ± 14.0	60.7 ± 14.8	>0.05*
Tumor localization (%)			
Colon	45.2	51.3	
Rectum	51.6	41.0	>0.05†
Colon and rectum	3.2	7.7	
Stage (%)			
1	12.9	2.6	
2	38.7	48.7	
3	25.8	38.4	>0.05†
4	16.1	10.3	
No defined stage	6.5	0	
Adjuvant treatment (%)			
No	64.5	61.5	
Yes	32.2	38.5	>0.05†
No record of treatment proposed	3.3	0	
Associated chronic diseases (%)			
No	48.4	38.5	>0.05†
Yes	51.6	61.5	

* Independent *t* test.
† Chi-square test.

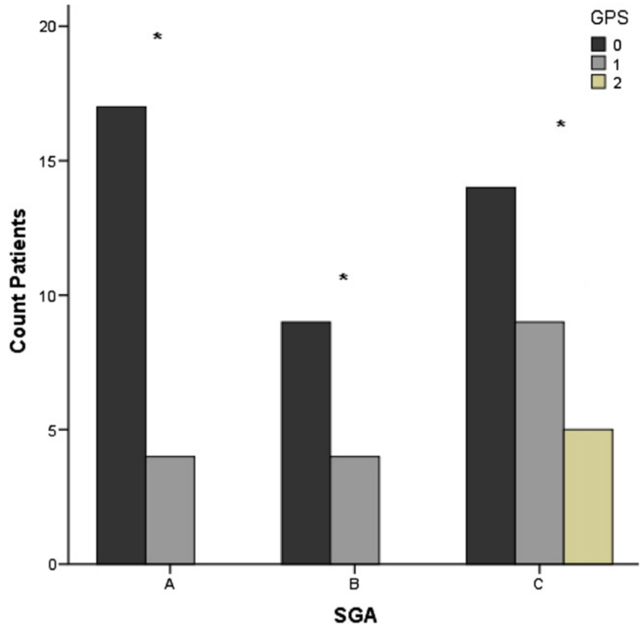

Fig. 1. Relation between nutritional status defined by the SGA and inflammation defined by the GPS in patients with colorectal cancer (chi-square test); Belo Horizonte, 2012. $^{*}P < 0.05$. GPS, Glasgow Prognostic Score; SGA, Subjective Global Assessment.

missing, which is reason they had no GPS determined. These data were missing because their blood tests were performed in outside laboratories and were not registered in the medical records. One hundred percent of patients with GPS 2 were classified as severely malnourished by the SGA, and 80.9% of the nourished patients were classified as GPS 0. GPS 1 was observed in 30.7% of patients with suspected malnutrition and in 32.1% of patients with severe malnutrition. There was a statistically significant association between the three SGA categories and the three GPS categories (chi-square = 7.16, $P < 0.05$). There was also a negative correlation between albumin and CRP (Spearman correlation, $r = -0.34$, $P < 0.05$).

The presence of complications was evaluated in 61 patients. Nine patients did not undergo the planned treatment or this was not documented until the end of data collection. Thus, such patients were not analyzed for the presence of complications. Of those who were analyzed, 37 patients (60.7%) had at least one complication. Many patients (39.3%) had diarrhea after the beginning of the antineoplastic treatment.

Table 2 presents the outcome data. Although malnourished patients (SGA B and C) had a higher prevalence of complications, there was no statistically significant difference between well-nourished and malnourished patients. The total number of patients in the GPS classes and those who had complications are presented in Table 3. All patients with GPS 2 had complications,

Table 2
Prevalence of complications among SGA groups; Belo Horizonte, 2012

	Total (n)	Patients with complications (n)	Prevalence (%)
SGA A	18	9	50.0
SGA B	16	10	62.5
SGA C	27	18	66.7

SGA, Subjective Global Assessment
Relation among groups A, B, and C, considering the SGA and frequency and prevalence of complications ($P > 0.05$, Fisher exact test).

Table 3
Prevalence of complications among GPS groups; Belo Horizonte, 2012

	Total (n)	Patients with complications (n)	Prevalence (%)
GPS 0	35	19	54.2
GPS 1	16	9	56.3
GPS 2	4	4	100

GPS, Glasgow Prognostic Score
Relation among groups 0, 1, and 2, considering the GPS and frequency and prevalence of complications ($P > 0.05$, Fisher exact test).

but there was no significant difference between the GPS classes and the presence of complications.

The overall prevalence of malnutrition varied depending on the method used for nutritional assessment. Table 4 presents the methods used to assess nutritional status and the respectively identified prevalence of malnutrition. All methods showed a lower prevalence of malnutrition compared with the SGA. The comparison among the anthropometric indicators (BMI, TSF, MAC, AMA, and APMT), body composition (body fat), PA, and muscle function (HGS) is presented in Table 5.

The values obtained with each tool differed significantly according to the SGA class. The Gabriel test was performed to compare each SGA class (A, B, and C) and showed that the BMI, TSF, MAC, AMA, APMT, percentage of body fat, PA, and HGS differed between nourished patients (SGA A) and severely malnourished patients (SGA C). Differences in MAC and AMA were also identified between classes of suspected or moderate malnutrition (SGA B) and severe malnutrition (SGA C). The BMI and MAC differed significantly between nourished patients (SGA A) and patients with suspected malnutrition or moderate malnutrition (SGA B). The MAC was the only parameter that differed significantly among all groups. Table 6 lists the κ index value for each assessed method. All indicators had low agreement with the SGA ($\kappa < 0.20$).

Discussion

This study enrolled 70 patients diagnosed with cancer of the colon and rectum. This is the first study to investigate the relation between nutritional status, defined by the SGA, and the severity of inflammation, assessed by the GPS, in patients with colorectal cancer. However, the relation between inflammation and nutritional status has been reported by others, who have used different tools and evaluated different types of cancer [19,20]. Giannousi et al. [21] found a significant association between nutritional status, defined by the Mini-Nutritional

Table 4
Methods to assess nutritional status and the respective prevalence of malnutrition; Belo Horizonte, 2012

Methods	Prevalence of malnutrition
SGA	70
AMA	58.9
MAC	52.9
BMI	31.4
PA	31.3
TSF	24.6
%BF	13.3
APMT	13.0
HGS	10.1

AMA, midarm muscle area; APMT, adductor pollicis muscle thickness; %BF, percentage of body fat; BMI, body mass index; HGS, handgrip strength; MAC, midarm circumference; PA, phase angle; SGA, Subjective Global Assessment; TSF, triceps skinfold

Table 5
Comparison between SGA groups and others indicators; Belo Horizonte, 2012

Variables	SGA A ($n = 21$)	SGA B ($n = 17$)	SGA C ($n = 32$)	P*
BMI	26.5 ± 3.1†	23.2 ± 2.7§	20.8 ± 4.1	<0.05
TSF	24.5 ± 10.9†	18.2 ± 10.0	14.1 ± 8.2	<0.05
MAC	30.5 ± 2.8†	27.8 ± 2.7§	24.6 ± 3.7‡	<0.05
AMA	34.3 ± 10.1†	30.8 ± 5.5	24.9 ± 7.3‡	<0.05
APMT	24.3 ± 4.2†	22.5 ± 6.5	20.0 ± 5.1	<0.05
%BF	32.5 ± 9.1†	26.3 ± 9.3	25.4 ± 7.7	<0.05
PA	5.5 ± 0.6†	5.4 ± 1.0	4.9 ± 1.1	<0.05
HGS	32.2 ± 13.5†	29.0 ± 10.4	24.3 ± 9.6	<0.05

AMA, midarm muscle area; APMT, adductor pollicis muscle thickness; %BF, percentage of body fat; BMI, body mass index; HGS, handgrip strength; MAC, midarm circumference; PA, phase angle; SGA, Subjective Global Assessment; TSF, triceps skinfold
Values are presented as mean ± SD (analysis of variance and Gabriel test).
* Analysis of variance.
† $P < 0.05$ (Gabriel test), differences between nourished patients (SGA A) and severely malnourished patients (SGA C).
‡ $P < 0.05$ (Gabriel test), differences between classes of suspected or moderate malnutrition (SGA B) and severe malnutrition (SGA C).
§ $P < 0.05$ (Gabriel test), differences between classes of nourished patients (SGA A) and patients with suspected malnutrition or moderate malnutrition (SGA B).

Assessment, and the proinflammatory state, defined by the GPS, in 122 patients with metastatic lung cancer. In univariate analysis, GPS and the Mini-Nutritional Assessment were significant predictors of survival, which was ratified by multivariate analysis. In a study by Read et al. [22], the relation between nutritional status and inflammation in 48 patients with advanced colorectal cancer was evaluated. In a univariate analysis, the investigators showed that various factors, including the SGA score and nutritional status, had significant prognostic value. They also found that patients classified as well-nourished had a significantly better survival than those classified as at risk or severely malnourished. There was a significant correlation between a CRP level higher than 10 mg/L and the SGA score produced by the patient. One possible explanation for this relation was described by Omran and Morley [23] who claimed that CRP is related to the nitrogen balance and therefore is an indirect reflection of malnutrition and catabolism.

The recognition that systemic inflammation plays a role in nutritional depletion can lead to the development of appropriate therapeutic strategies to decrease weight loss, which would increase treatment tolerance. The GPS may be a useful tool for screening patients who require nutritional interventions, and it may help determine which patients would better tolerate anticancer treatment. Worldwide, it is well known that many oncology centers do not have nutrition teams to help diagnose the nutritional status of all their patients. Thus, the score would allow the identification of those who would benefit from an early intervention. The GPS could be used as a complementary tool, because the SGA, which is essentially a clinical method, is superior for properly classifying a patient's nutritional state.

Table 6
The κ index values for the indicators evaluated; Belo Horizonte, 2012

SGA × indicators	κ Index	P
Midarm circumference	0.12	<0.05
Midarm muscle area	0.20	<0.05
Phase angle	0.11	<0.05
Handgrip strength	0.06	<0.05
Adductor pollicis muscle thickness	0.04	<0.05
Body mass index	0.05	<0.05
Triceps skinfold	0.09	<0.05
Body fat (%)	0.11	<0.05

SGA, Subjective Global Assessment
The κ index for each indicator evaluated showed a low agreement with the SGA (κ index <0.20).

The presence of inflammation and malnutrition, which are considered prognostic factors, is related to the complications and decreased survival in patients with cancer [24,25]. The study of nutritional and inflammatory states, two prognostic factors that are relatively "new," is of paramount importance for health, and it deserves more attention in future studies and in clinical practice. Andreyev et al. [26] carried out a retrospective study including 1555 patients with gastrointestinal cancer. These investigators reported that patients who lost weight at the start of chemotherapy had a worse response to treatment than patients without weight loss. They stated that a worse treatment outcome appears to occur in patients with weight loss because they receive significantly less chemotherapy and develop more toxicity, thus decreasing the tumor response to treatment. However, in the present study, the inflammatory state and nutritional status were not associated with the presence of complications. We believe that this association was not found because of the small sample. Furthermore, the present study, unlike others available in the literature [24,25,27], assessed not only patients with the disease in the advanced stages but also those with the disease in the early stages. The short follow-up time (3 mo) in our study also may have affected the results, lowering the probability of developing complications.

Another objective of the present study was to evaluate the nutritional status according to different methods of nutritional assessment and their relation with the SGA. In the present study, the prevalence of malnutrition was 70.1% according to the SGA. However, the prevalence of malnutrition defined by other methods was lower. Thus, we can assume that the SGA allows the identification of malnourished patients before body composition changes occur. Thus, the SGA, which is a clinical method, permits the evaluation of parameters that are not assessed early using objective methods, such as the way in which weight loss occurred (e.g., a decrease in food intake and gastrointestinal symptoms). Objective methods assess different body compartments and thus different levels or severities of malnutrition [15]. According to Barbosa-Silva et al. [15], the first level affected during the process of malnutrition is related to metabolic changes, such as those of cell membranes, which can be evaluated by the PA. Muscle function changes would be the next level affected, which could be evaluated by the APMT and HGS. Anthropometric parameters such as the BMI, TSF, MAC, and AMA would be the last level affected. Most of the time, this parameter is modified when malnutrition is advanced. Similar to the present study, Thoresen et al. [28] reported a high prevalence of sarcopenia, malnutrition, and cachexia in 77 patients with advanced colorectal carcinoma. These investigators assessed anthropometric parameters, sarcopenia, cachexia, nutritional risk, and SGA and found a lower agreement among different nutritional assessments. These findings may indicate that anthropometric indicators, body fat percentage, PA, and HGS could identify malnourished patients if other cutoff points are used. Moreover, in the literature, the cutoff points of anthropometric indicators specific to the population with neoplastic disease are not yet available. In contrast, Ramos Chaves et al. [29] found an agreement between the BMI and the patient-generated SGA. These investigators analyzed 450 non-selected patients with cancer at a radiotherapy referral center. Nutritional status assessment included recent weight changes, the BMI, and the patient-generated SGA.

Conclusion

Nutritional status defined by the SGA was associated with the GPS in patients with colorectal cancer. Complications were not related to nutritional status or the severity of inflammation. There was a rather small agreement between the different nutritional assessment methods and the SGA, which might have improved if other cutoff values had been adopted.

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