



Original/Cáncer

Malnutrition in patients with gastrointestinal cancer: effectiveness of different diagnostic methods

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Abstract

Objective: to estimate the effectiveness of methods for identifying the risk and/or presence of malnutrition in individuals with gastrointestinal neoplasia.

Methods: participated 143 patients with gastrointestinal cancer, cared for in the Oncology Clinic Infirmary of “Hospital Amaral Carvalho” (Jaú-SP). Excluded from the study were patients hospitalized in the intensive care unit, in a terminal state or those who had members amputated; those who had received blood transfusions during the last month; significant clinical bleeding; received endovenous albumin and uncontrolled infection. The nutritional status was classified according to the ratio between Real Weight and Habitual Weight, Body Mass Index, Nutritional Risk Index and Percent Adequacy. As the gold standard method the Scored Patient-Generated Subjective Global Assessment was used. The effectiveness of the methods for detecting the risk for or presence of malnutrition was evaluated. A ROC curve was constructed and its area (AUROC) was estimated. The areas were compared using z statistics. For each method the best cut-off point was established.

Results: of the patients, 74.1% presented an advanced stage of the disease, and 83.2% were undergoing chemotherapy treatment. All the methods showed adequate discriminatory capacity for detecting the risk of malnutrition and presence of malnutrition. The BMI was significantly better for detecting malnutrition than for the risk of malnutrition. The RW/HW was significantly better for detecting the risk of malnutrition than the other methods. The cut-off points were slightly lower than those recommended for the normative population for the methods RW/HW, NRI and Score %. For the BMI the cut-off point was higher than the recommended for the normative population.

Conclusion: the methods for evaluating nutritional status showed adequate discriminatory capacity for the

LA DESNUTRICIÓN EN PACIENTES CON CÁNCER GASTROINTESTINAL: EFECTIVIDAD DE DIFERENTES MÉTODOS DE DIAGNÓSTICO

Resumen

Objetivo: estimar la efectividad de los diferentes métodos para la identificación y/o presencia de desnutrición en las personas con riesgo de cáncer gastrointestinal.

Métodos: los participantes fueron 143 pacientes con cáncer gastrointestinal, atendidos en la sala del Hospital Clínico de Oncología Amaral Carvalho (Jau-SP). No se excluyeron los pacientes ingresados en la unidad de cuidados intensivos, con enfermedad terminal o con miembros amputados que recibieron transfusiones de sangre en el último mes, con hemorragias clínicamente relevantes, que recibieron albúmina intravenosa y aquellos con infección no controlada. El estado nutricional de los participantes se clasificó de acuerdo a la relación Peso Real y Peso Habitual (PR/PH), Índice de Masa Corporal (IMC), Índice de Riesgo Nutricional (IRN) y porcentaje de ajuste (% score). Como método estándar de oro se utilizó la Evaluación Global Subjetiva. Fue evaluada la eficacia de los métodos para detectar el riesgo de desnutrición o la presencia de desnutrición. La curva ROC fue construido y su área (AUROC) se estimó. Las áreas se compararon mediante z estadística. Para cada método resuelto el mejor punto de corte.

Resultados: de los pacientes, el 74,1% había avanzado en el estado de la enfermedad y el 83,2% fueron sometidos a métodos quimioterápicos. Todos los métodos de tratamiento mostraron una adecuada capacidad discriminatoria para detectar el riesgo de desnutrición y la presencia de la misma. El IMC fue significativamente mejor para la detección de la desnutrición que para el riesgo de desnutrición. El riesgo PR/PH fue significativamente mejor para detectar el riesgo de desnutrición que otros métodos. Los puntos de corte fueron inferiores a los puntos de corte recomendados para población normativa con los métodos PR/PH, NRI y porcentaje de ajuste (% score). Para el punto de corte del IMC fue mayor que el recomendado para la población normativa.

Conclusión: los métodos de evaluación del estado nutricional mostraron una capacidad discriminatoria ade-

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risk of malnutrition and presence of malnutrition in patients with gastrointestinal cancer.

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Introduction

Patients with gastrointestinal cancer are especially vulnerable to malnutrition¹⁻³ due to the peculiarities inherent to the disease. This type of cancer presents important effects on the digestive system, such as changes in intestinal transit, untreatable vomiting and early satiety, which act directly of the process of digestion and absorption of food⁴.

These systemic complications increase the patient's susceptibility to the development of neoplastic cachexia, which is characterized by progressive and involuntary weight loss that compromises the musculoskeletal system, leading to rapid loss of fatty tissue, atrophy of visceral organs and anergy⁵. Cachexia is capable of diminishing the quality of life and reducing the survival time of these patients².

Thus, with the aim of preventing or minimizing the effects of cachexia on the clinical status of patients with gastrointestinal cancer, the evaluation and follow-up of their nutritional status are essential. For this purpose, various methods have been used in clinical routine, such as anthropometry, biochemical data, and clinical and subjective evaluation^{6,7}.

Anthropometric measurements are widely used because they are simple to use and low cost methods^{6,8}. Laboratory measurements, in turn, are considered of great value as a complementary method for identifying nutritional implications, and therefore, are also commonly used in clinical practice^{9,10}.

As a specific method for the nutritional evaluation of patients with cancer, Ottery¹¹ proposed the Scored Patient-Generated Subjective Global Assessment (scored PG-SGA) method. This method consists of objective questions, with the purpose of investigating alterations in weight, ingestion of food, gastrointestinal symptoms and functional capacity. The first part of the instrument is filled out by the patient him/herself and the second by the health professional responsible for the case. Authors such as Isenring et al.¹², Barbosa-Silva⁶, Gómez Candela et al.¹³, Kim et al.¹⁴ and Vicente et al.¹⁵ have considered this method the gold standard and recommend it for the investigation of malnutrition in oncologic patients.

It should be pointed out, however, that for evaluating the risk of malnutrition and/or its presence, there are no consensually accepted and recommended criteria in the literature of this field. Therefore, this study was conducted, with the aim of estimating the effecti-

cuada del riesgo de desnutrición y de la presencia de desnutrición en pacientes con cáncer gastrointestinal.

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veness of different diagnostic methods for identifying the risk for and/or presence of malnutrition in individuals with gastrointestinal neoplasia.

Casuistic and Methods

Study and Sampling Design

This is a cross-sectional validation study. A non probabilistic sample design was adopted.

The participants in this study were patients with gastrointestinal cancer, over the age of 18 years, at the "Hospital Amaral Carvalho", Jaú-SP, Brazil, cared for in the Infirmary of the Oncology Clinic, in the period from November 2010 to October 2011, who agreed to the Terms of the Free and Informed Consent.

Gastrointestinal cancer was considered to be solid tumors such as those of the esophagus, stomach, small intestine, rectum, colon, exocrine pancreas, anus, hepatocarcinoma and biliary tract, in accordance with the proposal of the Brazilian Manual of Medical Oncology¹⁶.

The following exclusion criteria were adopted: Patients hospitalized in the intensive care unit, in a terminal state or with amputated limbs, those who had received a blood transfusion in the last month, who presented clinically significant bleeding (>1 tablespoonful a day), received endovenous albumin, and those who presented uncontrolled infection..

The choice of "Hospital Amaral Carvalho" for conducting this study was based on the fact that it is a recognized institution for cancer treatment in Brazil. The present study was approved by the Research Ethics Committee of the above-mentioned Hospital (CEPFHAC – 170/09).

Study Variables and Measurement Instruments

The nutritional status of the patients was estimated by different methods. The ratio between Real Weight and Habitual Weight (RW/HW), Body Mass Index (BMI), Nutritional Risk Index (NRI) and the Percent Adequacy (Score %) were calculated. As the gold standard method for the classification of risk for malnutrition of the patients the Scored Patient-Generated Subjective Global Assessment (scored PG-SGA) was used. These methods are described below.

Anthropometric Measurements

Weight (kg) was obtained using a fixed PL180 Filizola® scale with 100g precision. Habitual Weight was considered that related by the patient by means of the question “What was your habitual weight before you took ill?”.

For measurement of Real Height (m) the stadiometer fixed to the scale was used. The horizontal bar of the stadiometer was placed over the head of the patient, who was instructed to maintain his/her gaze coincident with the Frankfurt plane and feet, and buttocks and shoulders touching the ruler.

Brachial circumference (BC) (cm) was measured on the left arm, at the mid-point between the acromion process of the scapula and the olecranon of the ulna, with the use of a flexible, non-elastic metric tape. At the time of measurement, the upper limbs were positioned parallel to the patient’s trunk. The measurements were taken in triplicate and their arithmetic mean constituted the final measurement¹⁷.

To measure the tricipital cutaneous fold (TCF) (mm) a Harpenden® adipometer was used. The skin was raised 1 cm above the mid-point between the tip of the acromion process of the scapula and olecranon of the ulna. The measurement was taken on the midline of the posterior surface of the triceps with the arm and shoulder in a state of relaxation. The fold was parallel to the longitudinal axis of the arm¹⁷. After having obtained the BC and TCF measurements, the Arm Muscle Circumference (AMC) (mm) was estimated according to the proposal of Frisancho¹⁷ (Equation 1).

$$(1) \text{ Arm Muscle Circumference} = \text{Arm Circumference} - \pi (\text{Triceps Skin Fold})$$

The AMC was classified in accordance with the cut-off points proposed by Frisancho¹⁸ for patients of up to 74 years of age and as from 75 years of age, the classification of Burr and Phillips was considered¹⁹.

It should be explained that all the anthropometric measurements were taken by a researcher who had been duly calibrated in a pilot study ($\rho=0.92-0.98$)²⁰.

Laboratory Measurements

For the laboratory exams, the patient were informed that blood samples would be collected in the morning period, and that they should be at rest and fasting of 8-12 hours. The results of the hematologic exam and serum albumin components were obtained by consulting the record chart of each patient. The hematocrit and hemoglobin indicators were analyzed by microhaematocrit and cyanomethaemoglobin dosage. These values were interpreted in accordance with the proposal of Sauberlich et al.⁹.

Analyses for the total lymphocyte counts (TLC) or lymphocytometry were performed by the automated

electronic counter method and/or morphological evaluation in stained smears, and were then calculated using the percentage of lymphocytes and total Leucocyte counts²¹. The results were interpreted in accordance with the proposal of Grant et al.²¹.

Serum albumin was determined in the serum samples using Bromocresol Green (BCG) dye. The results were interpreted in accordance with the proposal of Cohn and Blackburn.²².

Nutritional Status Classification

For classification of the nutritional status by the ratio between the Real Weight and Habitual Weight (RW/HW) the reference proposed by Grant et al. was used²¹. The Body Mass Index (BMI) of the participants was calculated and classified according to age. For adult individuals under the age of 60 years, the cut-off points proposed by the World Health Organization were used;²³ and for adults over the age of 60 years the proposal of Lipschitz was considered²⁴.

The nutritional status was also calculated by means of the Nutritional Risk Index (NRI) (Equation 2) and it was classified in accordance with the proposal of *The Veterans Affairs Total Parenteral Nutrition Cooperative Study Group*²⁵.

$$(2) \quad \text{NRI} = [1.519 \cdot \text{serum albumin}(\text{g/l})] + \frac{0.417 \cdot (\text{RW}/100)}{\text{HW}}$$

In order to compute the Percent Adequacy (Score %) 4 anthropometric measurements (RW/HW, BMI, NRI and ACM) and 4 biochemical (hematocrit, hemoglobin, total lymphocyte count and albumin) measurements were used. Analysis was performed considering the sum of all the parameters in percent adequacy divided by the number of parameters evaluated (Equation 3). It was considered adequate when the individual attained 50 percent²⁶.

$$(3) \quad \text{Score\%} = \frac{\sum(\% \text{adequacy anthropometric and biochemical measures})}{n}$$

Patient-Generated-Subjective Global Assessment (PG-SGA score)

As gold standard for detecting the risk for malnutrition the Portuguese version of the ASG-PPP with the use of score, transculturally adapted by Gonzalez et al.²⁷ was applied. The individuals were classified in the categories “Well Nourished – Stage A”, “Moderately Undernourished or Suspected Malnutrition – Stage B” or “Severely Undernourished – Stage C” in accordance with the recommendations of Ottery²⁸.

Evaluation of the patients using the ASG-PPP score was performed by a single examiner, previously calibrated in a pilot study ($k=0.85$, $p=0.001$).

Statistical Planning

The anthropometric and biochemical measurements were estimated by point and by an interval of confidence of 95% ($IC_{95\%}$). The distribution of individuals according to sex and adequacy/inadequacy of the laboratory measurements (RV%) was evaluated and the association between these variables was studied, using the Chi-square test (χ^2).

To study the effectiveness of the different methods of evaluating nutritional status for detection of the risk for malnutrition and presence of undernourishment, the ROC curve was constructed and its area (AUROC) was estimated. The areas obtained by the different methods were compared using z statistics. For each method the best cut-off point was established; that is to say, the one that minimized the occurrence of errors (false positives and false negatives).

For the analyses, those individuals who were classified as Stage B and Stage C in the ASG-PPP score were considered at risk for undernourishment, and those who presented Stage C, were considered undernourished.

Results

In the period from November 2010 to October 2011, it was possible to evaluate 143 patients with gastrointestinal cancer. The participants' mean age was 57.4 (SD=9.6) years, with a minimum of 27 and maximum of 81 years of age, with 69.9% being of the male sex. The other demographic characteristics (marital status and educational level) of the patients were presented in detail in a previous study²⁹.

With regard to stage of the disease, 2 (1.4%) of the participants presented Stage I, 28 (19.6%) Stage II,

56 (39.1%) Stage III and 50 (35.0%) Stage IV. Seven (4.9%) patients presented no information about the staging of the disease at the time of evaluation, because the pathology had only recently been diagnosed or was excessively advanced.

Of the participants, 119 (83.2%) were submitted to chemotherapy treatment, 20 (14.0%) chemotherapy and concomitant radiotherapy and 4 (2.8%) were hospitalized because they presented some clinical inter-currence.

The anthropometric measures of the patients, according to sex, obtained during the nutritional evaluation, are presented in table I.

For both the male and female sex, there was no significant alteration in habitual and real body weight, but this was at the limit of significance.

Determination of laboratory measures (hematological and albumin) collected from patient record charts according to sex, are presented in table II.

A significantly higher proportion of patients of the male sex presented hematocrit and hemoglobin levels below the recommended values.

As regards nutritional status, according to the ASG-PPP score, 79 (55.2%) individuals were "Well Nourished", 46 (32.2%) "Moderately Undernourished or with Suspected Malnutrition" and 18 (12.6%) "Seriously Undernourished".

Figure 1 shows the distribution of patients according to the absence or presence of risk for malnutrition, and malnutrition estimated by the different methods (RW/HW, BMI, NRI, %Score and ASG-PPP Score) and the prevalence of malnutrition by 95% interval of confidence ($IC_{95\%}$).

Great disparity is noted in the identification of malnutrition when the different methods are used.

The (ROC) curves of the different methods of evaluating nutritional status for detection of the risk for

Table I
Descriptive statistics of anthropometric measurements of patients according to sex. Jaú, 2010-2011

Anthropometry***	Male		Female	
	Mean±SD*	$IC_{95\%}$ *	Mean±SD*	$IC_{95\%}$ *
Real Weight (actual) (kg)	67.57±15.86	64.46-70.68	60.48±14.30	56.20-64.75
Habitual Weight (kg)	75.65±16.50	72.42-78.88	68.40±14.92	63.94-72.86
Height (m)	1.68±0.06	1.66-1.69	1.54±0.06	1.52-1.56
AC (cm)	27.99±4.80	27.05-28.93	29.01±5.43	28.85-30.64
TCF (mm)	9.14±5.73	8.01-10.26	17.26±7.38	15.06-19.47
AMC (cm)	25.12±3.51	24.43-25.81	23.59±3.62	22.51-24.68
RW/HW	0.90±0.12	0.87-0.92	0.89±0.11	0.85-0.92
BMI (kg/m ²)	24.03±5.25	23.00-25.06	25.43±5.63	23.74-27.11
NRI	96.57±10.37	94.53-98.60	95.90±9.30	93.11-98.68

*SD: Standard Deviation, ** $IC_{95\%}$: 95% Interval of Confidence; ***BC: Brachial Circumference, TCF: Tricipital Cutaneous Fold, AMC: Arm Muscle Circumference, RW/HW: Ratio between Real Weight and Habitual Weight, BMI: Body Mass Index, NRI: Nutritional Risk Index.

Table II
Descriptive statistics of laboratory measurements of oncology patients according to sex. Jaú, 2010-2011

Measurements	Mean±SD*	IC _{95%} *	Minimum	Maximum	RV***	≥RV(n)	≥RV(n)	χ ²	p
Hematocrit (%)									
Male	36.26±5.01	35.28-37.24	25	50	≥44	4	96		
Female	35.29±3.30	34.31-36.28	29	42	≥38	10	33	12.624	<0.001 [#]
Hemoglobin (g/100ml)									
Male	11.87±1.75	11.52-12.21	8.1	16.0	≥14	13	87		
Female	11.52±1.17	11.17-11.87	8.5	13.4	≥12	16	27	10.901	0.001 [#]
Total Lymphocyte count (mm³)									
Male	2.238.88±873.35	2.067.70-2.410.06	580.00	5.226.00	>2.000	54	46		
Female	2.072.23±763.19	1.844.12-2.300.35	517.00	4.480.00	>2.000	20	23	0.675	0.411
Albumin (g/100ml)									
Male	3.90±0.54	3.79-4.00	2.4	5.2	>3.5	77	23		
Female	3.87±0.55	3.70-4.03	2.5	5.5	>3.5	30	13	0.835	0.361

*SD: Standard Deviation, **IC_{95%}: 95% Interval of Confidence ; ***RV: Reference Value. #statistically significant difference for α= 0.05.

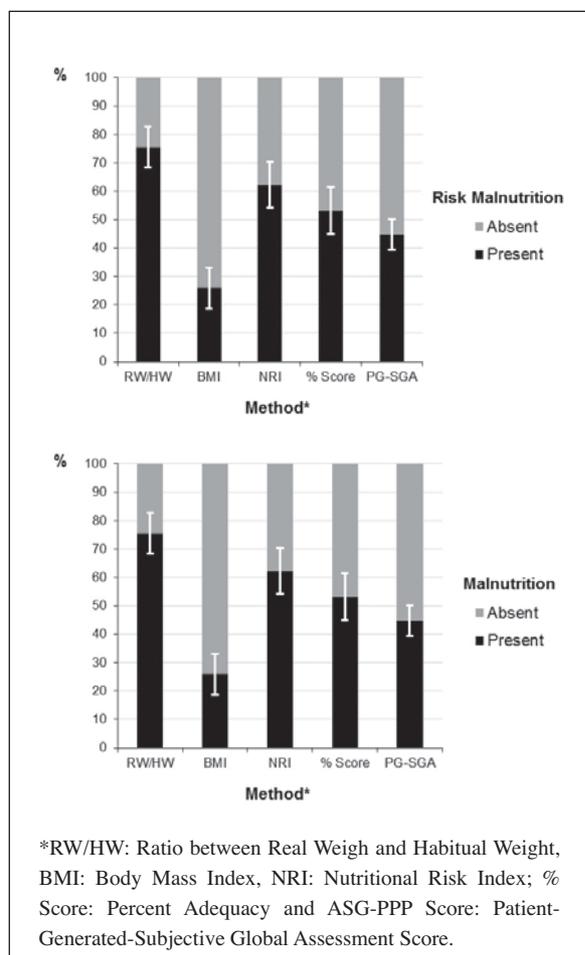


Fig. 1.—Distribution of patients according to absence or presence of risk of malnutrition, and malnutrition estimated by different methods. Jaú, 2010-2011.

malnutrition and presence of undernourishment, are shown in Figures 2 and 3 respectively.

All the methods presented adequate discriminatory capacity for detecting the risk for and presence of malnutrition.

The BMI was significantly better for detecting malnutrition than the risk for malnutrition. The RW/HW was significantly better for detecting the risk for malnutrition than the other methods.

The best cut-off point for each method and its sensitivity and specificity are shown in table III.

The cut-off points are slightly lower than the cut-off points recommended for the normative population for the RW/HW methods (≤ 0.95), NRI (≤ 100) and Percent Adequacy (< 50). For the BMI the cut-off point is higher than that recommended for the population ($< 18.5 \text{Kg/m}^2$).

Discussion

This study has contributed to the literature in the field of oncology, specifically in the case of gastrointestinal cancer, presenting the discriminatory capacity and cut-off points for detecting the risk for malnutrition and presence of undernourishment, as regards the use of the different methods of identifying the nutritional status commonly applied in clinical routine.

The prevalence of malnutrition found among patients evaluated by means of different diagnostic methods was significantly higher than that estimated using the gold standard (Figure 1). The identification of a larger number of individuals with malnutrition than the expected number may not represent a problem, because from the time that a larger number of

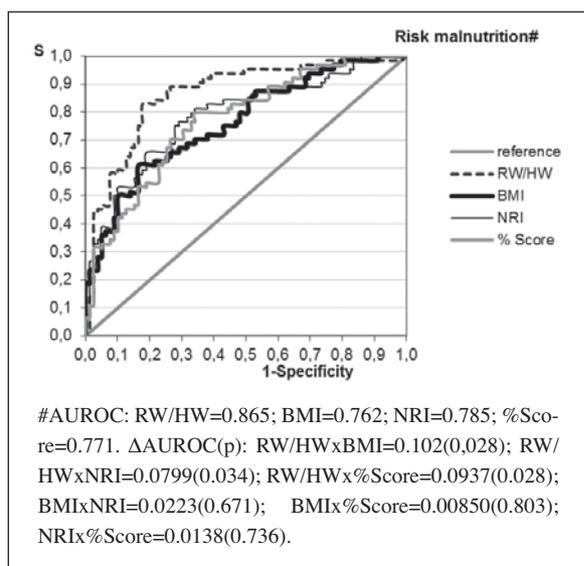


Fig. 2.—ROC Curve for different methods of diagnosing risk for Malnutrition. Jaú, 2010-2011.

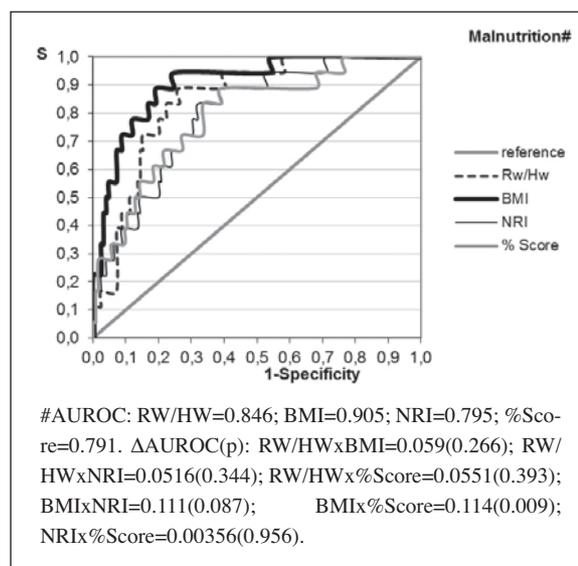


Fig. 3.—ROC Curve for different methods of diagnosing presence of Malnutrition. Jaú, 2010-2011.

individuals is identified, one has the opportunity to bringing them in for a more detailed clinical evaluation of their nutritional status, and thereby be able to act in a preventive manner.

All the methods evaluated presented adequate discriminatory capacity (Figures 2 and 3).

The ratio between real weight and habitual weight presented the capacity to discriminate the risk for malnutrition significantly better than the BMI and NRI methods (Figure 2). The BMI was significantly better for than the Percent Adequacy for detecting malnutrition (Figure 3).

These results may be interesting for clinical routine, because it is simpler and faster to compute both the RW/HW and BMI than to elaborate a protocol with multiple exams, as is the case with Percent Adequacy.

Nevertheless, it should be remembered that computing the RW/HW depends on information provided by the patient and/or present on the record chart, and

the BMI requires taking the weight and height measurements, and therefore, the oncology patient must present clinical conditions that favor the collection of this information and measurements⁶.

The good discriminatory capacity of the BMI for detecting malnutrition presented in the present study does not corroborate the results obtained by Vicente et al.¹⁵ who verified the low sensitivity of this method in the diagnosis of malnutrition (S=10.0 – 15.3%) in patients with gastric and colorectal cancer.

Another aspect that should be related is that the cut-off points for the RW/HW ratio, NRI and %Score used for identifying the risk for malnutrition and undernourishment in the patients evaluated were lower than those recommended for the normative population.

With regard to the laboratory measurements, the hematocrit and hemoglobin levels were below the reference values, particularly for the patients of the male sex. It could be speculated that this fact may be

Table III
Cut-off point of methods used for identifying patients at risk of malnutrition and undernourished patients. Jaú, 2010-2011

Methods***	Risk for Malnutrition			Malnutrition		
	Cut-off Point	S(%)*	Sp(%)**	Cut-off Point	S(%)*	Sp(%)**
RW/HW	0.90	82.81	82.28	0.85	88.89	73.60
BMI (kg/m ²)	21.37	60.94	83.54	20.36	88.89	80.80
NRI	97.37	76.56	70.89	94.44	83.33	68.00
%Score	50.23	79.69	65.82	47.98	83.33	66.40

*S: Sensitivity, **Sp: Specificity, ***RW/HW: Ratio between Real Weigh and Habitual Weight, BMI: Body Mass Index, NRI: Nutritional Risk Index; % Score: Percent Adequacy.

associated with the greater presence of risk factors for anemia, such as alcoholism in men, in addition to the possibility of the occurrence of bleeding arising from the neoplasias.

A limitation of this study was the sample size with reference to the group of severely undernourished patients shown by ASG-PPP, which resulted in an imbalance in the distribution of the nutritional status classification by this method, which may lead to a limitation of the power of analysis. In addition, the lack of homogeneity of the type of neoplasia and different stages of the disease presented by the patients could be considered a limitation.

The results pointed out that all the methods were adequate for detecting the risk for malnutrition and presence of undernourishments in patients with gastrointestinal cancer, when compared with the ASG-PPP Score. It should be emphasized that these methods present the advantages of simplicity, objectivity and speed, favoring their use in the clinical context. Therefore, it is suggested that the RW/HW and BMI methods should be used right after the patients' are admitted to hospital in order to rapidly trace the presence of the risk for malnutrition.

The methods for evaluation of the nutritional status, ratio between Real Weight and Habitual Weight (RW/HW), Body Mass Index (BMO), Nutritional Risk Index (NRI), and Percent Adequacy (%Score) presented adequate capacity to discriminate the risk of malnutrition and presence of undernourishment in patients with gastrointestinal cancer.

Author contributions

Prado, CD conducted the literature review, data collection, tabulation and contributed to the statistical analysis of data; Campos, JADB idealized the research project, performed the statistical analysis, carried out supervision of the execution of the work and the final wording of the text.

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