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O uso de diferentes indicadores de estado nutricional e sua relação com o desfecho clínico de pacientes oncológicos.

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LISTA DE ABREVIATURAS

IMC – Índice de Massa Corporal

ASG – Avaliação Subjetiva Global

AGG – PPP – Avaliação Subjetiva Global Produzida pelo Próprio Paciente

%PP – Percentual de Perda de Peso

OMS – Organização Mundial da Saúde

INCA – Instituto Nacional do Câncer

TGI – Trato Gastrointestinal

UICC – União Internacional Contra o Câncer

RR – Risco Relativo

EC – Estadiamento Clínico

GHC - Grupo Hospitalar Conceição

RESUMO

Introdução: O câncer é reconhecido como problema de saúde pública em todo o mundo. A alta prevalência de desnutrição em oncologia associa-se a maior morbimortalidade.

Objetivo: Correlacionar o estado nutricional de pacientes oncológicos, avaliado através de diferentes indicadores, com seus desfechos clínicos em 12 meses.

Métodos: Estudo retrospectivo e longitudinal, constituído por pacientes com câncer gastrintestinal hospitalizados em hospital público geral de Porto Alegre. Os dados foram obtidos através da revisão de prontuários eletrônicos e fichas de avaliação nutricional. O estado nutricional foi avaliado através dos indicadores: Índice de Massa Corporal (IMC), Avaliação Subjetiva Global Produzida Pelo Próprio Paciente (ASG-PPP) e Percentual de Perda de Peso (%PP). Os desfechos clínicos, nos 12 meses subseqüentes à primeira avaliação nutricional, foram classificados como positivos quando identificado tratamento concluído ou seguimento do tratamento, e como negativos quando identificado progressão de doença ou óbito.

Resultados: Foram avaliados 90 pacientes, sendo 55,6% deles do sexo masculino. A média de idade correspondeu a 59,7 ± 12,5 anos. Os diagnósticos predominantes foram câncer de cólon (28,9%) e reto (23,3%) e doenças em estágios avançados (37,8% em estadio III e 28,9% em IV), sendo 66,7% do tipo histológico adenocarcinoma. A desnutrição foi diagnosticada em 58,9% dos pacientes pela ASG-PPP, 27,8% pelo IMC e 53,3% pelo percentual de perda de peso. Encontrou-se boa concordância entre a ASG-PPP e o %PP ($k=0,62$; $p<0,001$). Quanto ao desfecho clínico, 47,8% apresentaram desfechos positivos e 52,2%, negativos. Encontram-se valores de associação significativos entre desnutrição e desfechos negativos ($p < 0,001$). Análise

ajustada para fatores de confusão demonstrou que a desnutrição estava associada com desfecho desfavorável.

Conclusão: O estado nutricional de pacientes com câncer gastrintestinal está relacionado com desfecho clínico apresentado em 12 meses. A desnutrição pode atuar negativamente sob o desfecho clínico do paciente oncológico.

Palavras-chave: desnutrição, estado nutricional, câncer, oncologia, neoplasias.

1 INTRODUÇÃO

O câncer é reconhecido como um problema de saúde pública em todo o mundo. De acordo com estimativas mundiais do projeto Globocan 2012, da *International Agency for Research on Cancer* da Organização Mundial da Saúde (Ferlay e cols., 2013), houve 14,1 milhões de casos novos de câncer e um total de 8,2 milhões de mortes por câncer, em todo o mundo, em 2012. No Brasil, a estimativa para o ano de 2015 aponta para a ocorrência de aproximadamente 576 mil novos casos, incluindo aqueles de câncer de pele não melanoma. As neoplasias malignas constituem a segunda causa de morte na população brasileira, sendo a prevenção dessas, uma das maiores dificuldades de saúde pública das últimas décadas (INCA, 2014).

O câncer caracteriza-se pelo crescimento descontrolado, rápido e invasivo de células com alteração em seu material genético. Muitos fatores influenciam o seu desenvolvimento, como o meio ambiente, os hábitos ou os costumes próprios de um determinado local, bem como os fatores internos, que são as causas geneticamente pré-determinadas (INCA, 2010).

Segundo estimativas do Instituto Nacional do Câncer (INCA), os tumores do trato digestório e respiratório figuram entre os de maior incidência no país. O câncer gástrico constitui a segunda causa de óbitos por câncer no mundo, enquanto o câncer de cólon e de reto atuam como a terceira causa mais comum de câncer em todo o mundo, em ambos os sexos, representando a quinta causa de morte por neoplasias. Na região Sul, o câncer de esôfago representa o quinto mais frequente entre homens (INCA, 2010).

Em indivíduos sadios, a taxa metabólica basal representa cerca de 60 a 70% do gasto energético diário, e em pacientes oncológicos o gasto energético de repouso pode variar entre 60 e 150% a mais que os níveis de normalidade, ou seja, o metabolismo energético alterado no câncer pode ser caracterizado por hipermetabolismo ou catabolismo persistente. Sendo assim, alterações na ingestão, no gasto energético e no metabolismo intensificam o comprometimento nutricional de pacientes com neoplasias malignas (Planas e cols., 2006).

Pacientes com câncer possuem um elevado requerimento nutricional devido à aceleração metabólica causada pelo tumor, que induz mudanças fisiopatológicas e altera as rotas metabólicas dos macronutrientes, promovendo catabolismo proteico aumentado, degradação muscular e aumento da oxidação lipídica. As principais alterações metabólicas observadas no paciente com câncer envolvem o estímulo da gliconeogênese a partir do lactato, o aumento da captação da glicose pelas células tumorais e a mobilização das reservas orgânicas (Guppy e cols., 2002). Fatores relacionados ao hospedeiro, como liberação de citocinas, aumento da taxa metabólica basal (que por sua vez aumenta o gasto energético total) e redução da ingestão alimentar, associados a fatores tumorais que incluem liberação de substâncias catabólicas, priorização de substratos energéticos e protéicos para a proliferação celular, podem ainda levar ao desenvolvimento da caquexia (Tisdale, 1997).

A caquexia é uma síndrome complexa e multifatorial, caracterizada pela perda grave de músculo esquelético e tecido adiposo, com consequente redução progressiva e involuntária de peso corporal, que está ligada a prognóstico adverso, com aumento da mortalidade (Inui, 2002). O quadro de

caquexia frequentemente é acompanhado pela anorexia, definida como perda de apetite. A anorexia é um sintoma comum em pacientes oncológicos. Em uma análise sistemática de pacientes com câncer avançado, ela aparece como o quarto sintoma mais relatado, ficando atrás apenas da dor, da fadiga e da fraqueza (Lagman e cols., 2005).

O prognóstico dos pacientes é adversamente afetado pela presença da anorexia, pois ela limita a ingestão alimentar. E, combinada à caquexia, induz perda de peso e de massa muscular (Blauwhoff-Buskermolen e cols., 2015). No estudo realizado por Lis e cols. em 2009, a anorexia foi identificada como um sintoma inversamente proporcional à qualidade de vida, independente de outros sintomas.

Diversos fatores podem ser considerados como possíveis causas da anorexia em câncer, a iniciar pelo impacto psicológico frente ao diagnóstico, que comumente causa sofrimento e perda de apetite. Além disso, a própria doença ativa gera uma resposta inflamatória que altera a função hipotalâmica, e, por sua vez, tem impacto sobre o apetite. Finalmente, os tratamentos antitumorais, como a quimioterapia e a radioterapia, costumam causar sintomas que afetam negativamente o apetite, a ingestão alimentar e a absorção de nutrientes, tais como náusea, vômito, diarréia, constipação, alteração de paladar e olfato, disfagia, odinofagia e xerostomia (Blauwhoff-Buskermolen e cols., 2015).

A prevalência de desnutrição descrita em pacientes portadores de câncer é de 20 a 80% (Menon e cols., 2014). Esta alta prevalência é preocupante, uma vez que está associada a maiores índices de morbidade e mortalidade, infecção, maior tempo de hospitalização, menor resposta ao

tratamento oncológico, maior custo hospitalar, redução da qualidade de vida e pior prognóstico da doença (Peres e cols., 2009).

No Brasil, a incidência de desnutrição em pacientes com câncer foi abordada em um estudo multicêntrico nacional chamado Ibranutri. O estudo avaliou 4.000 pacientes hospitalizados pelo Sistema Único de Saúde em hospitais de grandes cidades brasileiras e encontrou desnutrição presente em 47,6% dos enfermos. Nesta causística, 20,1% dos pacientes eram portadores de câncer. A prevalência de desnutrição nos pacientes oncológicos foi de 66,4%.

O estudo verificou que a presença de câncer foi considerada um fator de risco para a ocorrência de desnutrição, sendo o câncer associado a um aumento da ocorrência de desnutrição em 3,7 vezes. Pacientes com diagnóstico de câncer tiveram significativamente maior frequência de desnutrição que os pacientes sem câncer (66,3% versus 42,9%) (Waitzberg e cols., 2001).

Alguns fatores são determinantes na prevalência e na gravidade da desnutrição nos pacientes oncológicos, tais como o tipo de tumor, sua localização, o estágio da doença e o tratamento recebido. A maior prevalência de desnutrição é observada em pacientes com tumores do trato digestório (Menon, 2014).

Além dos malefícios já citados vinculados à desnutrição no paciente oncológico, soma-se o fato de que ao iniciarem o tratamento antineoplásico com o estado nutricional comprometido, os pacientes podem estar sujeitos a resultados desfavoráveis, como apresentar maior toxicidade às drogas quimioterápicas, complicações pós-operatórias e exacerbação dos efeitos

adversos da radioterapia. Isso pode predispor à piora de suas condições clínicas e até a interrupção do tratamento, o que torna desfavorável a sua evolução clínica (Fearon e cols., 2006).

A desnutrição pode se tornar uma condição tão desfavorável que alguns estudos apontam que 20% dos óbitos dos pacientes com câncer gastrointestinal ocorrem devido à desnutrição, e não devido à doença em si (Leuenberger e cols. 2010). Além disso, estima-se que, virtualmente, no momento do óbito, todos os pacientes oncológicos estejam desnutridos (Silva, 2004).

Estudos acerca da sobrevida de pacientes oncológicos sugerem que pacientes com menor sobrevida apresentam maior incidência de desnutrição, enquanto os maiores índices de sobrevida estão associados a pacientes obesos e eutróficos (Jamnik e cols., 2002).

A gênese, a progressão e a manutenção da desnutrição oncológica estão interligadas a múltiplos fatores etiológicos apresentados pelos pacientes com câncer. Este panorama multifatorial em que se encontra a desnutrição no câncer aponta para a importância de uma terapêutica nutricional adequada (Bosaeus e cols., 2002).

Dentro dessa perspectiva, a avaliação nutricional do paciente oncológico torna-se extremamente necessária para que intervenções precoces possam ser realizadas, visando a evolução clínica mais favorável e a melhor qualidade de vida desses, reduzindo os efeitos citotóxicos do tratamento e as suas complicações (Leuenberger e cols. 2010).

A avaliação nutricional é amplamente reconhecida por sua importância no acompanhamento hospitalar, direcionamento da conduta médica em todo

processo de hospitalização e investigação para corrigir deficiências nutricionais. Portanto, o objetivo da investigação do estado nutricional, além de detectar situações de risco nutricional, contribui para o planejamento dos cuidados médicos e representa uma ferramenta para fins prognósticos (Merhi e cols., 2007).

O estado nutricional dos pacientes é usualmente diagnosticado através da combinação de diversos indicadores; parâmetros clínicos, físicos, dietéticos, sociais, subjetivos, laboratoriais e antropométricos devem ser usados (Silva, 2004). Um dos métodos de avaliação nutricional utilizado na maioria dos hospitais é a chamada Avaliação Subjetiva Global (ASG). É um método clínico, em forma de questionário, considerado simples, de baixo custo e de grande aceitação na prática clínica (Detsky e cols.,1987).

Desde 1995 foi validada a utilização de uma adaptação da ASG, que é específica para pacientes oncológicos: a Avaliação Subjetiva Global Produzida Pelo Próprio Paciente (ASG-PPP), realizada por Ottery. Trata-se de um questionário auto-aplicativo, dividido em duas partes; a primeira respondida pelo paciente e a segunda, pelo profissional que o aplica. A diferença entre as duas consiste, basicamente, no acréscimo de informações específicas relacionadas ao câncer, com o objetivo de um melhor rastreamento do estado nutricional de pacientes oncológicos (Ottery, 1996).

Outros instrumentos de avaliação nutricional, essencialmente objetivos, são utilizados na prática clínica devido ao custo benefício, com destaque para o Índice de Massa Corporal (IMC), uma medida simples que relaciona o peso atual com a altura ao quadrado. Porém, devido a limitações, como a não distinção de massa gorda e magra, que pode levar à superestimação para

ambos os lados, não se recomenda o uso deste instrumento de forma isolada para avaliar o estado nutricional (Santos e Sichieri, 2005).

Em pacientes oncológicos, a perda de peso é considerada uma variável independente para avaliação prognóstica e para avaliação do estado nutricional (Andreyev e cols., 1998). Além disso, a perda de peso a partir do músculo esquelético é provavelmente o fator mais limitante para a sobrevida dos pacientes oncológicos, pois leva ao comprometimento de funções fisiológicas como diminuição da função respiratória e aumento da suscetibilidade a infecções (Windsor e cols., 1988; Fearon, 1992).

Uma perda de peso maior que 10% nos seis meses anteriores ao diagnóstico é considerada grave e representa um fator de risco independente para a sobrevida (Blackburn e Bistrian, 1977).

Assim, tem sido descrita uma prevalência elevada de desnutrição em pacientes com câncer. Sabe-se que o estado nutricional pode diferir de acordo com o indicador utilizado, e, ainda, que o comprometimento do estado nutricional se associa a maiores índices de morbimortalidade. Por isso, resolvemos identificar e correlacionar o estado nutricional desses pacientes, avaliado através de diferentes indicadores, com o desfecho clínico apresentado 12 meses após sua primeira avaliação.

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3 OBJETIVOS

Objetivo Primário

- Correlacionar o estado nutricional de pacientes oncológicos, avaliado através de diferentes indicadores, com seus desfechos clínicos 12 meses após a primeira avaliação, considerando o estadiamento e o tipo histológico da doença.

Objetivos Secundários

- Identificar o estado nutricional dos pacientes através de três diferentes indicadores de estado nutricional (ASG-PPP, IMC e %PP - percentual de perda de peso);
- Comparar os diferentes indicadores de estado nutricional, ASG-PPP, IMC e %PP.

4 ARTIGO CIENTÍFICO REDIGIDO EM INGLÊS

The use of different nutritional status indicators and their relation with clinical outcome of cancer patients

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ABSTRACT

Introduction: Cancer is worldwide recognized as a public health problem. Higher malnutrition ranks in cancer have been associated to higher morbimortality index.

Objective: To correlate nutritional status on cancer patients, through three different indicators, with the them clinical outcome on a 12-month period.

Methods: Retrospective and longitudinal study, formed by patients at Oncology unit of a public hospital from Porto Alegre, diagnosed with a digestive tract tumor. The data were collected by reviewing electronic medical records and nutritional assessment cards. The nutritional status was evaluated through of the Body Mass Index (BMI), Patient-Generated Subjective Global Assessment and Percentage (PG – SGA), Percentage Wheight Loss (PWL). Clinical outcomes, on a 12-month period after the first nutritional assessment date, were classified as positive outcome when identified follow up and under treatment condition, and as negative when identified disease progression or death.

Results: We evaluated 90 patients, which 55.6% were men. The mean age was 59.7 ± 12.5 years old. The predominant diagnose were colon (28.9%) and rectum (23.3%) cancer, and late-stage diseases, 37.8% in stage III and 28.9% in IV, which 66.7% were adenocarcinoma histologic type. Malnutrition was diagnosed in 58.9% of patients by PG – SGA, 27.8% by BMI and 53.3% by PWL. There was a good agreement only between PG–SGA and PWL (k=0.62; p<0.001). Regarding clinical outcome, 52.2% had negative outcomes. There were significant relation between malnutrition and negative outcomes (p <0.001). The adjusted analysis to confusing factors showed that malnutrition was associated with adverse outcome.

Conclusion: The nutritional status of gastrointestinal cancer patients is related with the clinical outcome presented on a 12-month period. Malnutrition may negatively act under clinical outcome of a cancer patient.

Key-words: malnutrition, nutritional status, cancer, oncology, tumor.

INTRODUCTION

Cancer is worldwide recognized as a public health problem. According to world estimates of the Globocan Project 2012, from International Agency of Research on Cancer of World Health Organization, there was a number of 14.1 million of recent cases of cancer and a total of 8.2 million deaths of cancer around the world in 2012, affecting people from all countries and regions[1].

Cancer patients have a high nutritional necessity due to metabolic acceleration caused by tumor, inducing pathophysiologic changes and redirecting metabolic pathways of macronutrients, thus promoting high protein catabolism, muscle damage and increasing lipid oxidation[2].

In healthy individuals, basal metabolic rate represents about 60 to 70% of daily energy waste. In cancer patients, energy waste in rest can be 60 to 150% higher, i.e., altered energy metabolism in cancer can be characterized by hypermetabolism or persistent catabolism. Thus, ingestion, energy waste and metabolism alterations intensify the nutritional engagement of patients with malignant tumor[3].

The presence of malnutrition in cancer patients ranges from 20 to 80%[4]. This information draws significant attention, once malnutrition is associated to major rates of morbimortality and infection, longer hospitalization period, shorter

reaction to oncology treatment, higher medical cost, life quality reduction and poor disease prognosis[5].

Furthermore, when an antineoplastic treatment is initiated in patients with damaged nutritional status, they can be liable to unfavorable results, showing greater levels of toxicity to chemotherapy drugs, post-surgery complications and exacerbation of radiotherapy adverse effects. Malnutrition might predispose to worse clinical conditions and even treatment breakup, resulting in an unfavorable positive clinical evolution[6].

The genesis, progress and maintenance of oncologic malnutrition are interconnected to multiple etiologic factors presented in cancer patients. This multifactorial outline in which cancer malnutrition is found aims to the importance of an adequate nutritional therapy[7].

Nutritional assessment is widely recognized by its importance in hospital monitoring, medical management direction throughout hospitalization process and investigation to correct nutritional flaws. Therefore, the investigation objective of nutritional status, besides detecting situations of nutritional risk, contributes to medical care planning and represents a tool for prognostic uses[8].

Nutritional status of patients is usually diagnosed through a combination of several indicators, that include clinical, physical, dietary, social, subjective, laboratory and anthropometric parameters[9].

Subjective Global Assessment (SGA) is one of the most nutritional status assessment used in hospitals. It was proposed by Detsky et al. in 1987[10]. However, since 1995, the use of an adaptated SGA, specific for cancer patients, has been validated; the Patient–Generated Subjective Global Assessment (PG – SGA). It was developed by Ottery in 1996[11]. The difference

between them basically lays on the addition of specific information related to cancer, aiming to obtaining a better tracking system of nutritional status on oncologic patients[5].

Body Mass Index (BMI) and Percentage Weight Loss (PWL) are essentially objective nutritional assessment instruments used in clinical practice due to their cost-benefit ratio. BMI is a simple measure relating current weight to height squared[12]. The Percentage Weight Loss is an anthropometric method that refers to weight change relating to usual weight and its evolution through time[13].

Therefore, the current study aims to identify and to correlate nutritional status of cancer patients, through three different nutritional status indicators (PG-SGA, BMI and PWL), with the clinical outcome of patients on a 12-month period after the first nutritional assessment, considering staging of disease and histological type.

METHODOLOGY

The current paper is a retrospective and longitudinal study, with patient sampling from Oncology centers from a local public hospital in Porto Alegre – South of Brazil, with histopathological diagnose of gastrointestinal (GI) tract tumor. The study was approved by the Institutional Ethics Committee.

The study included patients admitted to the oncology unit for the period from January 2011 to December 2012, older or equal to 20 years, of both sexes, without distinction of ethnicity, diagnosed with GI tract tumor in any clinical stage of the disease (stages 0 to IV) and who had been evaluated previously by the hospital Nutrition Service. The sample size was determined by

convenience, that is, the total number of patients hospitalized in the period and who met the inclusion criteria of the study.

The variables were collected by reviewing electronic medical records and nutritional evaluation forms. We collected the following data: sex, age, occupation, nutritional status diagnosed by PG-SGA, BMI and weight loss percentage; clinical outcome; clinical staging and histological classification of tumor.

The SGA used was that proposed by Ottery[11], the PG-SGA, specific for cancer patients, which rates patients in the following categories: well-nourished (SGA A), suspected of malnutrition or moderately malnourished (SGA B) and seriously malnourished (SGA C).

The reference pattern used for BMI was that proposed by World Health Organization (WHO) in 1995[14]. Thus, the patients who had BMI values from 18.5 to 24.9 kg/m² were classified as eutrophic; those with BMI lower than 18.5 kg/m² as low weight; those with BMI from 25 to 29.9 kg/m² as overweight, and finally those with BMI higher than or equal to 30 kg/m² were classified as obese.

For the weight loss assessment in the last six months, the weight loss was categorized by degrees: mild (< than 5%), moderate (from 5 to 10%) and severe (> than 10%)[10].

The clinical outcome was assessed individually 12 months after the first nutritional assessment date. The outcomes were classified as “follow up”, “under treatment”, “disease progression” or “death”. After that, they were grouped into positive and negative clinical outcomes: “follow up” and “under treatment” have been considered as positives outcomes, and “disease progression” and “death” as negatives outcomes.

The used staging system for tumor was that recommended by the International Union Against Cancer (UICC), called TNM Classification of Malignant Tumors. The system is based on the anatomical extent of disease (T), characteristics of nodes of the lymphatic drainage chains of the organ in which the tumor is located (C), and the presence or absence of distance metastases (M). These parameters receive graduations, usually from T0 to T4, N0 to N3, M0 and M1, respectively. Then, after gathering those signs, the staging was classified into 0 to IV variations[15]. The histological assessment was determined through histopathological exam, available through patient electronic records.

The categorical variables were shown by absolute and relative frequencies and the numeric variables by means and standard deviation. In order to evaluate the relationship and concordance among variables, Pearson Qui-squared test and a Kappa coefficient were applied respectively. In order to control confounding factors, Poisson regression analysis was applied. The effect measure used was the Relative Risk (RR) along with 95% of confidence interval. The variable input criteria on the multivariate model was a value of $p<0.20$ in the bivariate analysis. The adopted significance level was of 5% and the data statistic treatment was made by the SPSS (Statistical Package of the Social Sciences) program version 18.0.

RESULTS

We assessed 90 patients, including 40 women (44.4%) and 50 men (55.6%). The average age corresponded to 59.7 ± 12.5 years old, ranging from 35 to 85 years. In the professional environment, retired workers (28%) and

homeworkers (27%) prevailed, followed by stonemasons (12%) and rural workers (9%).

Table 1 describes the characterization of the sample regarding sex, diagnosis, clinical staging (CS) and histological assessment. The sample profile assessed was determined as a predominant senior population (74.4%), with larger prevalence of tumors located in intestinal colon (28.9%); moreover, the patients assessed presented diseases at a late stage (37.8% of the sample showed CS III and 28.9% CS IV).

As for different indicators of nutritional status assessed, Table 2 shows that the PG–SGA had an amount of malnutrition level (B and C diagnose) in 58.9% of patients; low weight at BMI occurred in 27.8% of the sample and when weight loss percentage was applied, malnutrition appears through levels of moderate and high weight loss in 53.3% of patients assessed.

In Table 3 are the results obtained through comparison of different nutritional status indicators. According to parameters adopted by Altman in 1991[16] to measure the agreement among variables, it was possible to say that a good agreement was found only between PG–SGA and PWL ($k = 0.62$; $p<0.001$). Although the agreement with PG–SGA had been noticeable ($p = 0.041$), comparing BMI to other parameters, the values of kappa coefficient were low.

Turning to clinical outcomes found, 25 patients (27.8%) were included in the “follow up”, 18 (20%) in the “under treatment”, 26 (28.9%) in the “death” and 21 (23.3%) in the “progression disease” category. Thus, if one gathers them in positive clinical outcomes (“follow up” + “under treatment”) and negative clinical

outcomes (“death” + “disease progression”), 43 patients had a positive clinical outcome (47.8%), while 47 (52.2%) had negative outcomes.

Table 4 shows the association of results obtained through different indicators of nutritional status with clinical outcomes grouped into positive and negative. Significant association values were found between diagnosed malnutrition through PG–SGA and mild and severe weight loss with negative outcomes ($p < 0.001$).

After adjusting possible confounding factors (staging, diagnose and histologic type) the parameters to evaluate nutritional status remain significantly associated with outcome (Table 5), proving that malnutrition was associated with unfavorable outcome (death or disease progression), irrespective of other clinical features.

DISCUSSION

In this study, we found a mean age of 59.7 ±12.5 years and prevalence of 57.7% senior patients. A similar result (a mean age 59.9 years) was taken by Merhi et al.[8], while investigating malnutrition in patients with digestive tract tumor. Oliveira Junior et al.[17] described that death risk by cancer increases gradually from the 5th life decade, reaching 71% when patients reach an average of 70-79 years. Such information is in agreement with the one identified in this paper, where high rates of death were stated, positioning itself as clinical outcome in 28.9% of the patients under evaluation.

Epidemiological studies indicate that age is one of the biggest risk factors for cancer development. In other words, cancer is age related, being more prominent in senior patients. Thus, with gradual increase of life expectancy,

cancer incidence has enhanced. This fact is understood as the increasing in the mutation probability to accumulate in the genetic material of each individual due to accumulate exposition to mutagenic factors[18].

Malnutrition and cancer are closely related, so that physiological changes resulting from this last condition can cause this compromised nutritional status and this, in turn, negatively influences the evolution of the disease and the treatment effectiveness. Acting in almost all organs and body systems, malnutrition is direct associated with the increased morbimortality of oncological patients[13,19].

Studies have been shown that the greatest prevalence of malnutrition is found in patients with localized disease in gastrointestinal tract[8,9,19]. Correia and Waitzberg[19] reported that the presence of a cancer increases the risk of malnutrition in 8.1 times, and when the tumor is located at GI tract, increase this risk to 15.7 times.

In this study, nutritional status was evaluated according to different indicators used in clinical practice. Malnutrition was diagnosed in 27.8% of patients by BMI, in 58.9% by PG–SGA and in 53.3% through PWL. Similar prevalence rates were found by Gupta et al.[20], Read et al.[21] and Conde et al.[22], that using PG-SGA, identified malnourished patients in 52%, 66% and 50%, of the cases.

The comparison between BMI and PG–SGA has been studied and reported widely in literature[23,24,25]. Which is possible to see on these comparisons, is that the PG-SGA is a good predictor of malnutrition due to their greater sensitivity. It is a quick, valid and reliable nutrition assessment tool that enables malnourished hospital patients with cancer to be identified and triaged for

nutrition support. On the after hand, BMI may underestimate the percentage of malnourished patients[26]. Also, unlike BMI, PG–SGA allows the identification of patients at risk of malnutrition before changes occur in the body surface and in anthropometric measures[5,26]. For these reasons, the use of BMI alone to assess the nutritional status is not recommended[12].

The unintentional weight loss has been used in oncology as a nutritional status indicator and an independent risk factor for the patients survival[5]. Even small weight loss percentage (less than 5% of body weight) before starting the cancer treatment are already associated with poor prognosis, and when greater than 10% six months prior to diagnosis, it is considered a serious and independent risk factor for survival[27,28,]. Acceptable loss variations in adults are 2% by weight in one month, 3.5% in three months and 5% in a period of six months; and any variation beyond these parameters is considered abnormal[29].

In the present study, moderate (between 5 and 10% of body weight) and severe (greater than 10%) weight loss were identified in 53.3% of patients, similar to the results described in the literature by Conde et al.[22] (53%) and by Segura et al.[30] (48.2%). Severe wheight loss was found by Nourissat et al.[31] in 30% of patients evaluated, a index also similar to that described in this paper, where the weight loss greater than 10% was reported in 31.1% of the study population.

Ottery et al.[11] state that the weight loss achieve 80 to 90% of patients with cancer at some stage of malignancy. Ravasco et al.[32] assessed the prevalence of malnutrition in cancer patients according to the stage of the disease and found that 10% of patients in stage I had lost more than 10% of its normal weight, while 85% of patients at stages III and IV had weight loss higher than

10%. This information shows that patients with diseases in advanced stages (III and IV) tend to have greater weight losses, which could explain the high percentage (66.7%) of malnutrition identified in this study.

Comparing the different nutritional status indicators, it was found that those who showed a significant association were the PWL and PG-SGA. BMI showed concordance with the PG-SGA, but it was a weak correlation, since the values of Kappa coefficient were low. Borges et al.[25] also reported, using BMI and SGA to assess cancer patients, that the results did not converge between both tools.

Regarding the association between nutritional status indicators and clinical outcomes showed after 12 months, we found a significant association between malnutrition evidenced by PG-SGA and weight loss with the outcomes 'disease progression' and 'death' (unfavorable outcomes). Similar results were reported in a retrospective study conducted in 2010 in the United States[33], where the found survival average of cancer malnourished patients was 15.5 and 9.7 months for patients classified as B and C in by PG-SGA, respectively; among well-nourished patients (PG-SGA A), this average was 19.3 months.

Jamnik et al.[34] also described a positive association between adverse clinical outcome and high weight loss, where 66.5% of patients with survival lower than or equal to one year had a more pronounced weight loss than those of the PWL group with a survival rate over five years (35.7%) ($p= 0.0029$). They also suggest that patients with lower survival have a higher incidence of malnutrition, while the highest survival rates are associated with obese and eutrophic patients. Another study aligned to this proposition found that malnourished patients with malignant tumors of the GI tract have worse prognosis than those well-fed or who was managed to stop the weight loss

process during treatment[28]. Such results are in agreement with this work and are consistent with the proposition that malnutrition in cancer patients leads to decreased response to anticancer treatment and more morbimortality[26].

. In conclusion, the nutritional status of patients with GI tract tumors is related with the clinical outcome presented on a 12-month period. Given this, it is evident the need for an early nutritional intervention to prevent, treat and/or reverse malnutrition, since this can be considered as a negative prognostic factor, because it is significantly associated with death and disease progression.

Finally, our core proposition as conclusion of this work is the inclusion of a specialized oncology nutrition service in all cancer treatment centers, early acting focused on the prevention of nutritional depletion in order to minimize the effects of the disease and treatment under the nutritional status.

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CONFLICT OF INTEREST

Conflict of interest statement: nothing to declare

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TABLE LEGENDS:

Table 1 - Description of the characteristics of age, sex, diagnosis, clinical staging and histological classification of patients with histological diagnosis gastrointestinal tract tumors (n = 90).

Table 2 - Description of the nutritional status of patients with histological diagnosis of gastrointestinal tract tumors, according to different indicators (n = 90).

Table 3 - Concordance between different indicators of nutritional status of patients with histological diagnosis of gastrointestinal tract tumors (n = 90).

Table 4 - Association of nutritional status indicators with the clinical outcomes of patients with histological diagnosis of gastrointestinal tract tumors (n = 90).

Table 5 - Effects of nutritional status indicators in unfavorable outcome of patients with histological diagnosis of gastrointestinal tract tumors (n = 90).

TABLES

Table 1

Variables	n (%)
Age (years)*	59.7 ± 12.5
Sex	
Female	40 (44.4)
Male	50 (55.6)
Diagnosis	
Intestinal Colon Cancer	26 (28.9)
Rectum Cancer	21 (23.3)
Anal Canal Cancer	16 (17.8)
Esophagus Cancer	12 (13.3)
Stomach Cancer	15 (16.7)
Clinical Staging	
I	9 (10.0)
II	21 (23.3)
III	34 (37.8)
IV	26 (28.9)
Histological Classification	
Adenocarcinoma	60 (66.7)
Epidermoid Carcinoma	30 (33.3)

* described by average ± standard deviation

Table 2

Variables	n (%)
PG-SGA	
A	37 (41.1)
B	45 (50.0)
C	8 (8.9)
BMI	
Underweight	25 (27.8)
Normal	44 (48.9)
Overweight	14 (15.6)
Obese	7 (7.8)
PWL	
No loss	12 (13.3)
Mild loss	30 (33.3)
Moderate loss	20 (22.2)
Severe loss	28 (31.1)

PG-SGA = Patient–Generated Subjective Global Assessment
PWL = Percentage Weight Loss
BMI = Body Mass Index

Table 3

Comparison	% Malnutrition	Kappa	Value of *p*
PG-SGA x PWL	58.9 x 53.3	0.618	<0.001
PG-SGA x BMI	58.9 x 27.8	0.176	0.041
PWL x BMI	53.3 x 27.8	0.115	0.208

PG-SGA = Patient–Generated Subjective Global Assessment
PWL = Percentage Weight Loss
BMI = Body Mass Index

Table 4

Variables	**Positive outcomes (n=43) n (%)**	**Negative outcomes (n=47) n (%)**	p
PG – SGA			<0.001
A	32 (74.4)	5 (10.6)	
B/C	11 (25.6)	42 (89.4)	
BMI			0.010
Under weight	6 (14.0)	19 (40.4)	
Others	37 (86.0)	28 (59.6)	
PWL			<0.001
No loss / Mild loss	36 (83.7)	6 (12.8)	
Moderate and severe loss	7 (16.3)	41 (87.2)	

PG-SGA = Patient–Generated Subjective Global Assessment
PWL = Percentage Weight Loss
BMI = Body Mass Index
Determined by Pearson Qui-Squared Test

Table 5

Variables	**Gross RR (IC 95%)**	**Adjusted* RR (IC 95%)**	p
PG-SGA (B/C)	5.86 (2.57 – 13.4)	5.14 (2.27 – 11.7)	<0.001
BMI (Low weight)	1.76 (1.24 – 2.52)	1.68 (1.19 – 2.38)	0.003
Moderate and severe PWL	5.98 (2.82 – 12.7)	4.89 (2.19 – 10.9)	<0.001

* adjusted to staging, diagnosis and histological type
PG-SGA = Patient–Generated Subjective Global Assessment
PWL = Percentage Weight Loss
BMI = Body Mass Index
Determined by Poisson Regression

5 CONSIDERAÇÕES FINAIS

O presente estudo foi aprovado pelo Comitê de Ética em Pesquisa do Grupo Hospitalar Conceição (GHC) sob o parecer de número 194.764 (em anexo).

O Serviço de Oncologia do GHC é um centro de referência no tratamento de pacientes com câncer, conta com uma equipe multidisciplinar de assistência e com um programa de Residência Integrada Multiprofissional em Saúde, garantindo o cuidado integral do paciente. O vínculo entre uma instituição de ensino, a UFCSPA, e um hospital que acolhe pacientes oncológicos pelo Sistema Único de Saúde, no caso o GHC, é extremamente promissor.

O aprimoramento do conhecimento na área da Nutrição Oncológica visa uma melhor compreensão dos mecanismos envolvidos na terapêutica nutricional do paciente, como também dos fatores prognósticos que influenciam o seu desfecho clínico; desta forma, novos e promissores achados científicos podem contribuir para um melhor tratamento do paciente com câncer.

6 ANEXOS

5.1 Parecer do Comitê de Ética em Pesquisa

GRUPO HOSPITALAR CONCEIÇÃO/HOSPITAL NOSSA SENHORA DA

PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: Avaliação de diferentes indicadores de estado nutricional e sua relação com o desfecho clínico de pacientes oncológicos.

Pesquisador: Camila Feijó Borges

Área Temática:

Versão: 4

CAAE: 09120712.7.0000.5530

Instituição Proponente: Grupo Hospitalar Conceição/Hospital Nossa Senhora da Conceição S.A.

Patrocinador Principal: Financiamento Próprio

DADOS DO PARECER

Número do Parecer: 194.794

Data da Relatoria: 09/01/2013

Apresentação do Projeto:

-

Objetivo da Pesquisa:

OBJETIVO PRIMÁRIO

Avaliar os resultados obtidos através da utilização de diferentes indicadores de estado nutricional, comparando-os entre si e relacionando-os com o desfecho clínico de pacientes portadores de neoplasias malignas do trato gastrintestinal internados no serviço de Oncologia do Hospital Nossa Senhora da Conceição, Porto Alegre ¿ RS.

OBJETIVOS SECUNDÁRIOS

- Identificar o estado nutricional dos pacientes incluídos no estudo através de três diferentes indicadores de estado nutricional (ASG-PPP, IMC e %PP - percentual de perda de peso);
- Comparar entre si os resultados obtidos através dos diferentes indicadores de estado nutricional;
- Relacionar os resultados obtidos através dos diferentes indicadores de estado nutricional com o

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desfecho clínico dos pacientes no período de 12 meses, considerando estadiamento e tipo histológico da doença.

Avaliação dos Riscos e Benefícios:

-

Comentários e Considerações sobre a Pesquisa:

-

Considerações sobre os Termos de apresentação obrigatória:

-

Recomendações:

-

Conclusões ou Pendências e Lista de Inadequações:

Pendências resolvidas

Situação do Parecer:

Aprovado

Necessita Apreciação da CONEP:

Não

Considerações Finais a critério do CEP:

PORTO ALEGRE, 06 de Fevereiro de 2013

Assinador por:
Daniela Montano Wilhelms
(Coordenador)