Longitudinal assessment of nutritional risk in patients under chemo or radiotherapy

Isabelle Mastelaro[1], Mariana Pietrobom Pupin[1], Sofia Miranda de Figueiredo Ribeiro[2], Harley Francisco de Oliveira[3], Fernanda Maris Peria[3], Selma Freire de Carvalho da Cunha[4]*

[1]Undergraduate Student of the Nutrition and Metabolism Program, Universidade de São Paulo (USP), São Paulo, SP, Brazil
[2]MSc – PhD Student, USP, São Paulo, SP, Brazil
[3]PhD Professor, Division of Clinical Oncology, Faculdade de Medicina de Ribeirão Preto, USP, Ribeirão Preto, SP, Brazil
[4]PhD Professor, Division of Nutrology, Faculdade de Medicina de Ribeirão Preto, USP, Ribeirão Preto, SP, Brazil

Summary

Objective: To compare nutritional risk in adult patients undergoing chemotherapy and radiotherapy in the beginning, middle, and end of oncologic treatment.
Method: This prospective, comparative study included 83 adult patients, 44 undergoing chemotherapy (CT group) and 39 undergoing radiotherapy (RT group) at an oncology treatment center. Nutritional risk was determined by NRS-2002 in the beginning, middle, and end of therapy. Statistical analysis was performed using Statistica 8.0 software.
Results: No differences in food intake or body mass index were observed between the CT (24.6±4.8 kg/m²) and RT groups (25.0±5.9 kg/m², p=0.75). Weight loss in the preceding 3 months was detected in 56.8% of CT group and 38.5% of RT group (p=0.09). The weight loss percentage compared with the usual weight within 3 months was greater (p<0.001) in the CT (11.4±6.5%) than in the RT group (3.9±6.8%). In the beginning of treatment, we observed high percentages of patients at moderate (18.2 *vs.* 15.4%, p=0.73) and high nutritional risk (61.4 *vs.* 48.7%, p=0.25), with no statistical difference between the CT and RT groups, respectively. During therapy, the nutritional risk remained unaltered in both groups. In the end of therapy, the majority of patients were at moderate (18.2 *vs.* 12.8%, p=0.50) or severe nutritional risk (50.0 *vs.* 51.3%, p=0.91), in the CT and RT groups, respectively, regardless of the type of oncologic treatment.
Conclusion: The high prevalence of patients at moderate or high nutritional risk in the beginning of treatment indicates the need for an early and continuous follow-up of the nutritional status of patients undergoing oncologic treatment.

Keywords: chemotherapy, radiotherapy, nutritional assessment, neoplasms, malnutrition, nutritional status.

Study conducted at Hospital das Clínicas, Faculdade de Medicina de Ribeirão Preto, Universidade de São Paulo (FMUSP Ribeirão Preto), Ribeirão Preto, SP, Brazil

Article received: 7/28/2015
Accepted for publication: 10/19/2015

***Correspondence:**
Address: Av. Bandeirantes, 3900, s/n
Ribeirão Preto, SP – Brazil
Postal code: 14048-900
sfreire@fmrp.usp.br

http://dx.doi.org/10.1590/1806-9282.62.07.659

Introduction

The prevalence of malnutrition in cancer patients ranges from 30 to 80%[1] depending on the criteria used to define malnutrition, the site, type, and staging of the tumor, as well as the treatment's modality.[2] Malnutrition increases morbidity, mortality, costs to health and may cause intolerance and inadequate response to anti-cancer therapy.[3] Identifying and addressing the nutritional problems are essential for an early and proper treatment of patients undergoing cancer therapy. However, nutritional assessment is not a priority in cancer services so that malnutrition is often undiagnosed.[4,5]

Routine nutritional assessment is recommended to identify patients at nutritional risk, and uses validated tools for cancer patients.[5] The nutritional screening tools were created to identify quickly and easily individuals

in various stages of nutritional deficiency. One of these tools is the Nutritional Risk Screening-2002 (NRS-2002), recommended by the European Society for Parenteral and Enteral Nutrition (ESPEN).[6] The NRS-2002 can be applied to patients with various morbid conditions,[7] including cancer.

Worsening of nutritional status during the oncological therapy has been described[8] as a result of a combination of factors related to the tumor and toxicity of the treatment itself.[9] In this context, the objective of this study was to compare the nutritional risk in adult patients undergoing chemo and radiotherapy at the beginning, middle, and at the time of completion of cancer treatment.

Method

This prospective, descriptive study was approved by the Research Ethics Committee (Process 15822/2011) and conducted in the cancer treatment unit of a Brazilian public university hospital. Data collection was done by two trained evaluators from a convenience sample consisting of adult patients who started cancer treatment, excluding those under simultaneous chemo and radiotherapy. All subjects who agreed to voluntary participate in the study were included, even those with physical, cognitive or emotional disabilities, which could hinder the communication between patient and evaluator.

The sample included 83 patients with cancer in the upper gastrointestinal tract (n=14), lower gastrointestinal tract (n=12), head and neck (n=12), bronchi or lungs (n=11), breast (n=11), urological (n=10), and other tumor sites (n=13). The subjects were grouped according to oncological treatment modality, with 44 patients undergoing chemotherapy (CT group) and 39, radiotherapy (RT group). There was no statistical difference in age (59.8±15.7 *vs.* 59.8±12.7 years, p=0.98) or percentage of male gender (54.6 *vs.* 69.2%, p=0.17) between the CT and RT groups, respectively. The distribution of individuals according to tumor site, habits, and living conditions was similar between groups, except for the largest number of people with alcohol abuse history among those treated with radiotherapy (22.7 *vs.* 46.1%, p=0.02).

The volunteers were evaluated based on the NRS-2002 protocol, which analyzed body mass index (BMI), recent weight loss history, changes in food intake and severity of the underlying disease.[6] Body weight was measured on an electronic scale for adults (Welmy® W200), with an accuracy of 100 g and a maximum capacity of 200 kg. Patients were weighed standing up straight, barefoot and with minimal clothing. Height was obtained from records in the patient's chart or measured using a graded metal rod with a maximum length of 2.0 m and accuracy of 0.5 cm. The BMI was calculated based on the formula: weight in kilograms divided by height in meters squared (kg/m^2). The patient and/or his guardian were asked about any unintentional weight loss in the prior 3 months and changes in food intake in the week before the evaluation.

Normal nutritional status was defined as the absence of weight loss < 5% and changes in food consumption. We considered low nutritional risk when the patient had one of the following criteria: a) weight loss > 5% in 3 months; b) food intake below the range 50 to 75% of normal needs in the previous week. Moderate nutritional risk was if the patient had two of the following criteria: a) weight loss > 5% in 2 months; b) BMI between 18.5 and 20.5 kg/m^2 in the presence of impairment of general condition; c) food consumption from 25 to 50% of normal needs in the previous week. And severe nutritional risk was if the patient had three of the following criteria: a) weight loss > 5% in 1 month (or > 15% in 3 months); b) BMI < 18.5 kg/m^2 associated with overall poor health; c) food intake below 25% of normal needs in the previous week. The final score was obtained by adding an additional point, considering that all patients had a diagnosis of cancer. According to the NRS-2002 questionnaire guidelines, we added a point to the previous items for patients older than 70 years.

The nutritional screening protocol was applied by two trained evaluators on three occasions, namely the first day, the middle, and the end of the oncologic treatment. Given that the average duration of chemotherapy was 90 days, the patients in the CT group were reevaluated in the 45th and 90th day. The radiation scheme included five weekly sessions for 6 weeks, so that patients in the RT group were reevaluated in the 15th and 30th day after the start of cancer treatment. In addition, at the beginning of treatment, the patients were asked about the number of daily meals, the consistency of the preferred food preparations, and changes in the pattern of consumption of food groups.

Statistical analysis was performed using Statistica software (version 8.0; StatSoft Inc, Tulsa, OK, USA). The comparative analysis was made by Student's t test. Numerical data are presented as mean and standard deviation; categorical data are presented as frequency. In all analyzes, the significance level was 5%.

Results

The initial assessment showed that both the anthropometric data and changes in food intake were similar between groups (Table 1). Compared to the RT group, a larger number of patients in the CT group showed weight loss in the first and second months before the start of

cancer treatment. Considering the individuals who lost weight, only, the percentage of weight loss was higher in the CT group in the first, second and third months before treatment. Analyzing the two groups together, 48.2% of patients had weight loss greater or equal to 5% over 3 months prior to evaluation.

TABLE 1 Criteria evaluated at the beginning of the study, according to oncological treatment modality, based on the questionnaire NRS-2002.

	CT group (n=44)	RT group (n=39)	p-value
Anthropometric data			
Usual weight (kg)	72.3±14.3	71.2±15.6	0.72
Current weight (kg)	66.8±15	68.5±16.8	0.61
Height (m)	1.64±0.09	1.65±0.08	0.52
BMI (kg/m²)	24.6±4.8	25±5.9	0.75
History of weight loss in 3 months			
Cases [n (%)]	25 (56.8)	15 (38.5)	0.09
Weight lost (kg)	7.9±4.6	2.6±4.3	<0.001
Loss percentage (%)	11.4±6.5	3.9±6.8	<0.001
History of weight loss in 2 months			
Cases [n (%)]	12 (27.3)	5 (12.8)	<0.001
Weight lost (kg)	5.8±5.3	0.5±1.4	<0.001
Loss percentage (%)	6.2±3.8	0.8±2.3	<0.001
History of weight loss in 1 month			
Cases [n (%)]	20 (45.4)	7 (17.9)	0.008
Weight lost (kg)	2.5±2.1	0.7±1.9	0.002
Loss percentage (%)	3.4±2.3	0.9±2.5	<0.001
Food intake compared to the usual			
> 75% [n (%)]	22 (50)	22 (56.4)	0.56
51 to 75% [n (%)]	10 (22.7)	3 (7.7)	0.06
26 to 50% [n (%)]	8 (18.2)	11 (28.2)	0.28
0 to 25% [n (%)]	4 (9.1)	3 (7.7)	0.82

BMI: body mass index; CT: chemotherapy; RT: radiotherapy.

TABLE 2 Nutritional risk in patients undergoing chemo or radiotherapy, according to the period of cancer treatment.

	CT group (n=44)	RT group (n=39)	p-value
Beginning of treatment			
Low risk	9 (20.4%)	14 (35.9%)	0.12
Moderate risk	8 (18.2%)	6 (15.4%)	0.73
Severe risk	27 (61.4%)	19 (48.7%)	0.25
Middle of therapy			
Low risk	15 (34.1%)	14 (35.9%)	0.86
Moderate risk	7 (15.9%)	8 (20.5%)	0.59
Severe risk	22 (50%)	17 (43.6%)	0.56
End of therapy			
Low risk	14 (31.8%)	14 (35.9%)	0.69
Moderate risk	8 (18.2%)	5 (12.8%)	0.50
Severe risk	22 (50%)	20 (51.3%)	0.91

CT: chemotherapy; RT: radiotherapy.

TABLE 3 Features of food intake in patients undergoing chemo or radiotherapy.

	CT group (n=44)	RT group (n=39)	p-value
Number of meals	4.0±1.0	4.2±1.1	0.42
Food consistency			
Solid [n, (%)]	40 (91.0)	32 (82)	0.91
Pasty [n, (%)]	2 (4.5)	2 (5)	0.57
Liquid [n, (%)]	2 (4.5)	5 (13)	0.37
Reduced intake of food groups			
Green leafy vegetables [n, (%)]	11 (25.0)	3 (7.7)	0.03
Other vegetables [n, (%)]	5 (11.4)	4 (10.3)	0.87
Cereals [n, (%)]	9 (20.4)	6 (15.4)	0.55
Meat [n, (%)]	11 (25.0)	11 (28.2)	0.74
Dairy [n, (%)]	4 (9.1)	2 (5.1)	0.48

CT: chemotherapy; RT: radiotherapy.

In the longitudinal comparison within each group (beginning, middle and end), there was no difference in the occurrence of mild, moderate or severe nutritional risks among the patients in the two study groups (Table 2). The NRS-2002 reveals a high prevalence of moderate or high nutritional risk in the first (79.6 *vs.* 64.1%), second (65.9 *vs.* 64.1%), and third (68.2 *vs.* 64.1%) assessments among the patients in the CT and RT groups, respectively.

There was no statistical difference in the number of daily meals and food consistency among the groups (Table 3). Patients undergoing chemotherapy reported a reduction in the consumption of vegetables. When asked about a reason for this change, patients reported having received guidance from their treating physician, aimed at preventing infections related to microbiological contamination of raw foods. In both groups, about 25% of patients reported a reduction in meat intake, justified by the difficulty in chewing, nausea and vomiting, and changes in taste and smell.

Discussion

Although BMI and history of reduction in food intake were similar at baseline, this study documented the highest percentage of weight loss in patients undergoing chemotherapy compared to those under radiotherapy. At

baseline, moderate or severe nutritional risk scores were similar and high in both groups, remaining relatively constant until the end of treatment. The patients consumed four meals daily, preferably eating solid foods and reducing meat consumption. The patients undergoing chemotherapy showed greater reduction in consumption of vegetables compared to those treated with radiotherapy.

In this study, a large number of patients experienced moderate or severe nutritional risk at the start of chemotherapy (79.6%) and radiotherapy (64.1%). In the sequential evaluation, the patients maintained this nutritional risk until the end of treatment, so that severe risk occurred in 50% of cases under chemotherapy and 51.3% of those undergoing radiotherapy. The prevalence of compromised nutritional status in our study is consistent with results of studies by other researchers.[10-13] Based on the NRS-2002, severe nutritional risk was documented in 50% of patients before the start of cancer treatment[13] and in 76% of individuals with various types of cancers.[11] Among patients recently hospitalized with various types of cancer, the use of Patient-Generated Subjective Global Assessment protocol showed varying degrees of malnutrition in about 70% of cases.[10,12] In Australia, the risk of malnutrition was documented in 64% of patients admitted to a public hospital specializing in cancer treatment,[14] but only in 17% of cases treated in an outpatient oncology unit.[5]

Female gender and age were associated with nutritional risk.[13] Patients hospitalized with cancer have higher nutritional risk rates[10,12] than those seen in the oncologic treatment center.[5,8] There is a difference in the prevalence of severe malnutrition, ranging 17 to 43% of the cases evaluated. Such differences may be attributed to different tumor sites, as seen in the study by Fernández-López (2013),[12] which included patients with tumors in the head and neck, pancreas, lung, and lower and upper gastrointestinal tract, while Bauer et al. (2002)[10] assessed patients with lymphoma, myeloma, sarcoma, breast cancer, prostate cancer, esophageal, and lung cancer.

In this study, weight loss greater or equal to 5% in the previous 3 months was documented in 48.2% of cases, regardless of the mode of cancer treatment. These results are similar to those documented in patients recently admitted to the oncology department of a general hospital in Mexico, where weight loss greater than 5% occurred in 40.3% of cases, stratified as mild loss (8.8%), moderate (9.7%) or severe (21.8%).[13] Nevertheless, Fernández-López et al. (2013)[12] documented that 69% of cancer patients in their sample lost more than 5% of their usual weight over the 3 months prior to treatment with the highest frequency among those with tumors of the digestive tract. Weight loss, anorexia,[15] and dysphagia[16] occur commonly in cancer, particularly in advanced stages and tumors in locations that compromise food intake.

In our study, food intake less than 50% from the usual consumption occurred in 27.3 and 35.9% of patients undergoing chemotherapy and radiotherapy, respectively. Similar results have been documented in newly hospitalized cancer patients with moderate to severe food intake impairment in 56% of cases.[13] In patients at cancer centers, limited food consumption varied between 10 and 80%,[8] attributed to complaints of nausea and vomiting,[8,12] as well as early satiety.[12]

A limitation of our study is that the patients had various types of cancer, which hampers a comprehensive analysis of the results, considering that patients with cancer in the upper and lower digestive system and tumors of the head and neck are at greater nutritional risk.[17,18] On the other hand, the strength of our study was the application of three sequential evaluations during treatment, which allowed us to identify high nutritional risk at the beginning of cancer therapy. Our results suggest that dietary/nutritional measures should be implemented from the start of cancer treatment, aiming to improve the nutritional status or even prevent its deterioration. In developed countries, most malnourished patients in cancer centers do not receive nutritional guidance.[8] The inclusion of nutrition professionals in oncology services will allow early nutritional guidance, including nutritional therapy, if necessary.[11] The diet's nutritional value, feeding frequency, and consistency of the food can affect the severity of gastrointestinal symptoms and cause negative impact on food intake, nutritional status, and quality of life.[16] For example, patients can be instructed to drink pasty or liquid foods, eating fractionated meals and in small volumes,[16] or to fortify their diet and use nutritional supplements orally.[19]

The fact that the nutritional risk of the patients in our study was maintained without deterioration can be seen as a positive aspect of the service, as there are reports of worsened nutritional status during cancer treatment.[8] Our results can be attributed to individual dietary guidance given by the researchers, including delivery of written material containing basic information and general dietary behaviors to minimize food complaints during the oncological treatment. In addition, where necessary, the patients were referred to outpatient care specialized in enteral nutrition. Still, we believe that nutritional risk could have been further reduced if specialized dietary guidance and early enteral nutrition therapy were deployed.

We found a high prevalence of moderate or severe nutritional risk at the start of chemotherapy and radio-

therapy and this scenario was maintained during and after treatment. It is well documented that inadequate nutritional intake is involved in maintaining the nutritional risk during cancer treatment. In the last decade, it has been postulated that inflammation plays a central role in the cachexia of cancer, based on studies showing the effects of inflammatory mediators such as TNF-alpha, IFN-gamma, IL-1, IL-6.[19-21] In this context, in addition to nutritional counseling with the purpose of reducing the nutritional risk, a major scientific challenge in this area is to develop studies evaluating the effect of specific nutrients to reduce inflammatory cytokines involved in the etiology of neoplastic cachexia.

Resumo

Avaliação longitudinal do risco nutricional em pacientes sob quimio ou radioterapia

Objetivo: comparar o risco nutricional de pacientes adultos submetidos a quimio e radioterapia no início, no meio e ao término do tratamento oncológico.
Método: estudo prospectivo e comparativo conduzido com 83 pacientes adultos de um centro de tratamento oncológico, sendo 44 sujeitos sob quimioterapia (grupo QTx) e 39 sob radioterapia (grupo RTx). O risco nutricional foi determinado pelo questionário NRS-2002 no início, ao meio e ao término da terapia. A análise estatística foi feita com o software Statistica 8.0.
Resultados: não houve diferença no padrão de ingestão alimentar e no IMC (24,6±4,8 *vs.* 25±5,9 kg/m²; p=0,75) nos grupos QTx e RTx, respectivamente. Perda de peso nos 3 meses precedentes ocorreu em 56,8% dos pacientes sob quimioterapia e em 38,5% daqueles sob radioterapia (p=0,09). Os pacientes do grupo QTx apresentaram maior porcentagem de perda de peso em relação ao habitual em 3 meses (11,4±6,5 *vs.* 3,9±6,8%; p<0,001). No início do tratamento, houve alta taxa de risco nutricional moderado (18,2 *vs.* 15,4%; p=0,73) e grave (61,4 *vs.* 48,7%; p=0,25), sem diferença estatística entre os grupos QTx e RTx, respectivamente. No meio do tratamento, o risco nutricional foi mantido em ambos os grupos. Ao término da terapia, mais da metade dos pacientes apresentava risco nutricional moderado (18,2 *vs.* 12,8%; p=0,50) ou grave (50 *vs.* 51,3%; p=0,91), independentemente da modalidade de tratamento oncológico.
Conclusão: a alta prevalência de risco nutricional moderado ou grave no início do tratamento aponta para a necessidade de abordagem nutricional precoce e permanente durante a terapia oncológica.

Palavras-chave: quimioterapia, radioterapia, avaliação nutricional, neoplasias, desnutrição, estado nutricional.

References

1. Barthelemy N, Streel S, Donneau AF, Coucke P, Albert A , Guillaume M. Screening for malnutrition in lung cancer patients undergoing radiotherapy. Support Care Cancer. 2014; 22(6):1531-6.
2. Vandebroek AJV, Schrijvers D. Nutritional issues in anti-cancer treatment. Ann Oncol. 2008; 19(Suppl 5):v52-5.
3. Ehrsson YT, Langius-Eklöf A, Laurell G. Nutritional surveillance and weight loss in head and neck cancer patients. Support Care Cancer. 2012; 20(4):757-65.
4. Wie GA, Cho YA, Kim SY, Kim SM, Bae JM, Joung H. Prevalence and risk factors of malnutrition among cancer patients according to tumor location and stage in the National Cancer Center in Korea. Nutrition. 2010; 26(3):263-8.
5. Abbott J, Teleni L, McKavanagh D, Watson J, McCarthy A, Isenring E. A novel, automated nutrition screening system as a predictor of nutritional risk in an oncology day treatment unit (ODTU). Support Care Cancer. 2014; 22(8):2107-12.
6. Kondrup J, Rasmussen HH, Hamberg O, Stanga Z; Ad Hoc ESPEN Working Group. Nutritional risk screening (NRS 2002): a new method based on an analysis of controlled clinical trials. Clin Nutr. 2003; 22(3):321-36.
7. Raslan M, Gonzalez MC, Dias MCG, Paes-Barbosa FC, Cecconello I, Waitzberg DL. Applicability of nutritional screening methods in hospitalized patients. Rev Nutr. 2008; 21(5):553-61.
8. Davidson W, Teleni L, Muller J, Ferguson M, McCarthy AL, Vick J, et al. Malnutrition and chemotherapy-induced nausea and vomiting: implications for practice. Oncol Nurs Forum. 2012; 39(4):E340-5.
9. Lu ZH, Yang L, Yu JW, Lu M, Li J, Zhou J, et al. Weight loss correlates with macrophage inhibitory cytokine-1 expression and might influence outcome in patients with advanced esophageal squamous cell carcinoma. Asian Pac J Cancer Prev. 2014; 15(15):6047-52.
10. Bauer J, Capra S, Ferguson M. Use of the scored Patient-Generated Subjective Global Assessment (PG-SGA) as a nutrition assessment tool in patients with cancer. Eur J Clin Nutr. 2002; 56(8):779-85.
11. Bozzetti F, Mariani L, Lo Vullo S; SCRINIO Working Group, Amerio ML, Biffi R, et al. The nutritional risk in oncology: a study of 1,453 cancer outpatients. Support Care Cancer. 2012; 20(8):1919-28.
12. Fernández-López MT, Saenz Fernández CA, de Sás Prada MT, Alonso Urrutia S, Bardasco Alonso ML, Alves Pérez MT, et al. [Malnutrition in patients with cancer; four years experience]. Nutr Hosp. 2013; 28(2):372-81.
13. Alvarez-Altamirano K, Delgadillo T, García-García A, Alatriste-Ortiz G, Fuchs-Tarlovsky V. [Prevalence of nutritional risk evaluated with NRS-2002 in Mexican oncology population]. Nutr Hosp. 2014; 30(1):173-8.
14. Boltong AG, Loeliger JM, Steer BL. Using a public hospital funding model to strengthen a case for improved nutritional care in a cancer setting. Aust Health Rev. 2013; 37(3):286-90.
15. Paoli S, Fonseca AS, Paoli F, Geller M, Presta GA, Santos-Filho SD, et al. A review of scientific papers about head and neck cancers. Braz Arch Biol Technol. 2008; 51:63-9.
16. Kapala A, Lange E. Possibility of pain reduction by dietary intervention in patients with advanced cancer. Ann Agric Environ Med. 2013; Spec no. 1:18-22.
17. Righini CA, Timi N, Junet P, Bertolo A, Reyt E, Atallah I. Assessment of nutritional status at the time of diagnosis in patients treated for head and neck cancer. Eur Ann Otorhinolaryngol Head Neck Dis. 2013; 130(1):8-14.
18. Shaw C, Fleuret C, Pickard JM, Mohammed K, Black G, Wedlake L. Comparison of a novel, simple nutrition screening tool for adult oncology inpatients and the Malnutrition Screening Tool (MST) against the Patient-Generated Subjective Global Assessment (PG-SGA). Support Care Cancer. 2015; 23(1):47-54.
19. Sánchez-Muñoz A, Pérez-Ruiz E, Sáez MI, Trigo JM, Galindo MM, Manzaneque L, et al. Limited impact of palliative chemotherapy on survival in advanced solid tumours in patients with poor performance status. Clin Transl Oncol. 2011; 13(6):426-9.
20. Argilés JM, Busquets S, Toledo M, López-Soriano FJ. The role of cytokines in cancer cachexia. Curr Opin Support Palliat Care. 2009; 3(4):263-8.
21. Skipworth RJ, Stewart GD, Dejong CH, Preston T, Fearon KC. Pathophysiology of cancer cachexia: much more than host-tumour interaction? Clin Nutr. 2007; 26(6):667-76.