Original Article

Effects of use of food supplements increased with omega-3 on nutritional status in patients with gastrointestinal tract neoplasia evaluated by computed tomography

Efeitos do uso de suplementação alimentar acrescido de ômega-3 sob o estado nutricional em pacientes com neoplasia do trato gastrointestinal avaliados por tomografia computadorizada

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ABSTRACT

Introduction: Patients with gastrointestinal cancer are more susceptible to malnutrition when compared to other patients. Omega-3 supplements are being widely investigated for their effect on clinical progression, modulation of the inflammatory and immunological response, improvement of sarcopenia, nutritional status, and body composition. The aim of this study was to evaluate the effect of the use of high-calorie and high-protein dietary supplementation with omega-3 on the nutritional status of patients with gastrointestinal cancer. **Methods:** This was a longitudinal quantitative study. The study included 12 adult patients with gastrointestinal cancer, undergoing chemotherapy and radiotherapy, and who used high-calorie and high-protein dietary supplementation with omega-3. The parameters evaluated were anthropometric assessment, subjective global assessment and body composition by computed tomography. The patients were followed up for three months. **Results:** All patients used the proposed supplementation, even when experiencing complications during the treatment process, and were able to stabilize weight loss and body composition. **Conclusion:** Hypercaloric and hyperproteic supplementation with omega-3 demonstrated positive effects in aiding the treatment of patients with gastrointestinal tract cancer, mainly in meeting nutritional demands, maintaining muscle mass and mitigating weight loss. These factors are directly linked to the patient's recovery during and after cancer treatment.

RESUMO

Introdução: Pacientes oncológicos do trato gastrointestinal são mais suscetíveis à desnutrição quando comparados a outros pacientes. Suplementos de ômega-3 estão sendo amplamente investigados quanto ao seu efeito na evolução clínica, na modulação da resposta inflamatória e imunológica, na melhora da sarcopenia, estado nutricional e composição corporal. O objetivo deste estudo foi avaliar o efeito do uso da suplementação alimentar hipercalórica e hiperproteica acrescida de ômega-3 no estado nutricional de pacientes portadores de neoplasia do trato gastrointestinal. **Método:** Este foi um estudo longitudinal de caráter quantitativo. Na pesquisa, foram incluídos 12 pacientes adultos, portadores de neoplasia do trato gastrointestinal, em tratamento quimioterápico e radioterápico, que utilizaram suplemento alimentar hipercalórico e hiperprotéico acrescido de ômega-3. Os parâmetros avaliados foram avaliação antropométrica, avaliação subjetiva global e composição corporal pela tomografia computadorizada. Os pacientes foram acompanhados por três meses. **Resultados:** Todos utilizaram a suplementação proposta. Mesmo passando por complicações dentro do processo de tratamento, os pacientes conseguiram estabilizar a perda de peso e a composição corporal. **Conclusão:** A suplementação hipercalórica e hiperproteica acrescida com ômega-3 demonstrou resultados positivos no auxílio do tratamento de pacientes com câncer do trato gastrointestinal, principalmente para atingir as demandas nutricionais, manutenção da musculatura e atenuação da perda de peso. Esses fatores estão diretamente ligados com a recuperação do paciente durante e após o tratamento oncológico.

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INTRODUCTION

Malnutrition is a common feature in cancer patients and is caused by the presence of the tumor and medical and surgical anticancer treatments. Malnutrition negatively impacts quality of life, the immune system and tolerance of treatment. It is estimated that 10 to 20% of cancer patients die due to the consequences of malnutrition, and not from the tumor itself[1]. Furthermore, malnutrition is linked to sarcopenia, causing decreased lean body mass and muscle performance. Weight loss and skeletal muscle mass are hallmarks of cancer sarcopenia, a progressive and irreversible process in patients with advanced neoplasia[2].

Thus, nutrition plays an essential role in the multimodal treatment of cancer. Nutritional issues must be taken into account from the moment of diagnosis and should occur in parallel with oncological treatment[1]. Therefore, the assessment of nutritional status, including lean mass and adipose tissue, is important for an accurate diagnosis and for an adequate and personalized nutritional intervention, increasing survival rates, nutritional status, food intake, functional capacity and quality of life. For nutritional therapy, the oral route is preferred, with emphasis on the use of nutritional supplements combined with oral feeding as an alternative to meet dietary demands in situations where food intake does not meet nutritional needs (60% to 70%/day)[3].

Caloric intake combined with omega-3, in adequate quantity and quality, has been recommended as part of nutritional therapy, to promote the gain or preservation of muscle mass, weight and, consequently, improvements in the quality of life and prognosis in cancer patients[4].

Therefore, the objective of this study was to evaluate the impact of hypercaloric and hyperprotein supplementation with omega-3 on the body composition of oncology patients of the gastrointestinal tract, using computed tomography.

METHODS

This is a longitudinal quantitative study in which patients with potential participation were selected by the oncologist at the first consultation, who referred them to the researcher responsible for the nutrition department. Non-random convenience sampling was used to select participants, considering all patients who met the study eligibility criteria. The sample consisted of patients over 18 years of age, of both sexes, diagnosed with gastrointestinal tract neoplasms, who had experienced weight loss in the last three months prior to diagnosis and were scheduled to begin chemotherapy treatment, with or without radiotherapy.

Patients who did not meet the inclusion criteria, such as those without recent weight loss, pregnant women, or those with health conditions that could interfere with participation in the study, such as cognitive impairment or use of alternative feeding methods, were excluded from the study. In addition, patients who did not consent to participate or who did not complete the study were excluded. The research took place in person at the oncology service of Hospital Bruno Born from August 2021 to April 2022.

Nutritional care and the first data collection were performed one week after the patient had undergone the first computed tomography (CT) scan. In the first nutritional assessment, the patient's anamnesis and anthropometric assessment were performed, collecting data on weight, height, body mass index (BMI) and calf circunference (CC). After obtaining these data, the Subjective Global Assessment (SGA) was performed, an instrument validated as the gold standard for assessing the nutritional status of cancer patients subjectively, considering functional changes and changes in the patient's body composition[3].

To establish body composition, CT scans were performed using a Canon Medical Systems Corporation Aquilion Prime TSX-303A 80-channel CT scanner. The Vitrea Enterprise software was used to reproduce the images and calculate the body area of muscle mass and fat. The first CT scan used to assess body composition was the same as the one used at the beginning of each patient's oncological treatment, marking the beginning of the assessments and nutritional intervention. A second CT scan was performed three months later, which marked the end of the nutritional intervention.

The CT scans used for this study measured the area of subcutaneous fat, visceral fat and muscle area in centimeters. The muscle area was corrected for muscle mass index (MMI; muscle area/height^2 in cm/m^2), as described in the literature. The area of muscle mass measured by CT is linearly related to whole-body skeletal muscle when normalized for height[5]. The images were acquired from the scout, with fifteen two-millimeter slices at the level of the third and fourth lumbar vertebrae (L3 and L4) through the cross-sectional view and specific software, as illustrated by Figure 1.

Patients who had some degree of weight loss prior to treatment were eligible to receive high-calorie, high-protein oral dietary supplementation with omega-3. The product used in this study was a dietary supplement intended for adult cancer patients, containing omega-3 (DHA and EPA) of animal origin, with proteins and without flavor. The supplement was free of sucrose, glucose, fructose and lactose, and can be diluted in liquids or added to food preparations. In addition, its composition included minerals such as calcium, iron, copper, zinc, selenium, and vitamins A, D, E, K and C. The supplement was delivered in sachets containing 30 g each. The standard prescribed amount was 60 g/day as indicated by the laboratory. Along with the supplement, patients received a prescription with the correct amount to be used and an e-book with recipes

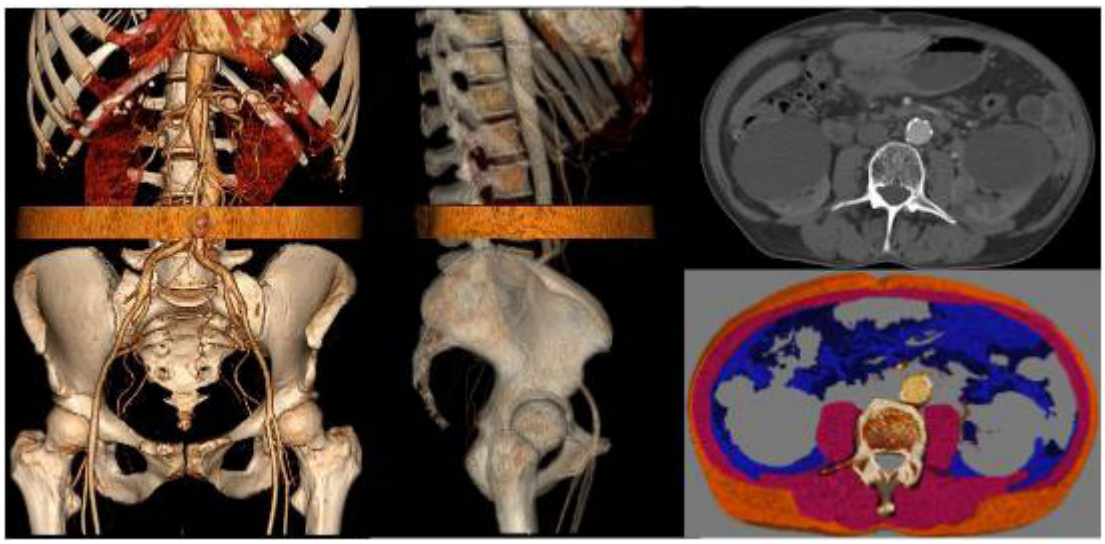

Figure 1 - *Example of axial CT slice at L3 and L4 for assessment of body composition using software.*

to include the supplement in their daily routine. Each patient received the number of sachets stipulated for one month of individual use during the consultations.

During the three months of nutritional intervention, participants attended three complete nutritional assessment appointments, one each month. During these appointments, patients were reassessed using the same methods applied in the first assessment. At each follow-up appointment, participants submitted records of the number of sachets consumed at home throughout the month, which were verified and recorded with the aim of analyzing adherence to the proposed nutritional therapy.

It is important to highlight that during the intervention, some changes which were not initially anticipated occurred in the prescription of the supplement for certain patients. These changes occurred in two situations. Firstly, the patient's nutritional status was deteriorating rapidly due to the symptoms of the cancer treatment and the aggressiveness of the disease. To avoid greater harm to his health, it was necessary to increase the supply of the study supplement in order to minimize weight loss and avoid the need for another nutritional intervention. In the second situation, the patient was not tolerating the prescribed volume, but, since his nutritional status was stable according to the nutritional assessment, it was decided to reduce the amount of the daily supplement.

For statistical analysis, the collected data were stored in an Excel spreadsheet. Statistical analysis was performed using the JAMOVI and R Core Team statistical programs. The Kolmogorov Smirnov and Shapiro-Wilk tests were used to verify data normality. The parametric samples analyzed in the related groups (pre- and post-intervention) were expressed as mean ± standard deviation using the t-test for paired samples. The pre- and post-intervention variables of the following variables were compared: muscle area (cm^2), MMI (cm^2/m^2), visceral fat (cm^2), subcutaneous fat (cm^2), total fat area (cm^2), CC and BMI. To assess whether there was an association between the nominal variable SGA-PPP between before and after the intervention, the McNemar test was used. Cohen's D was calculated to demonstrate the effect size, considering classes of <0.2 (small effect), >0.2 to 0.49 (medium effect) and >0.5 (large effect). The value of $p<0.05$ was considered statistically significant for all analyses and confidence interval (CI) used was 95%.

For this study, the consent form was signed and the research was approved by the research ethics committee of the University of Vale do Taquari under number 4,710,004. After the end of the data collection period, established at 10 months, the research was finalized.

RESULTS

Twelve patients were measured, 6 (50%) men and 6 (50%) women. The overall mean age was 67.5±12.2 years. All patients had a diagnosis of gastrointestinal tract neoplasia and underwent chemotherapy alone or combined chemotherapy/radiotherapy. During oncological treatment, 8 of the 12 patients presented complications resulting from the treatments, such as diarrhea, vomiting, fatigue, asthenia, nausea, loss of appetite and even the need for hospitalization.

In a comparative analysis, regarding BMI, 7 patients were classified as underweight and 5 patients as eutrophic, according to the 2002 PAHO classifications[6], after nutritional

intervention. Regarding CC, before nutritional intervention, 7 of the 12 patients had a value below the cutoff point recommended by the Asian Working Group on Sarcopenia to predict sarcopenia or low appendicular skeletal muscle mass in men (≤34 cm) and women (≤33 cm)[7]. However, after nutritional intervention, only 5 patients presented values below the recommended level.

The images obtained through CT measured visceral fat, adipose tissue and muscle tissue. In the case of visceral fat and subcutaneous fat (that is, the total fat area), in a comparative analysis before and after the intervention, of the 12 patients, 7 showed an increase in this index, 1 patient showed no difference and 4 patients showed a reduction in this index. Regarding muscle tissue, at the end of the intervention, 6 patients increased the muscle area and 6 reduced this index by a minimum percentage.

The MMI cutoff points used in this study, specific for cancer patients established by Prado et al.[5] were separated by sex, being 52.4 cm^2/m^2 for men and 38.5 cm^2/m^2 for women. Patients below these values were classified as having sarcopenia. In total, between men and women, before the nutritional intervention, 4 patients were classified as sarcopenic. After the intervention, 5 patients were classified as sarcopenic. However, from the statistically paired analyses, no significant differences were observed between before and after the intervention, for any of the investigated variables (Table 1). This was also observed for SGA-PPP, which had no association between the pre- and post-intervention period ($X^2=4.0$; df=3; p=0.26; Table 2).

Regarding the high-calorie and high-protein dietary supplementation with omega-3, all patients started using 60 g/day as prescribed by the study, equivalent to a total of 265 calories, 18 g of protein and 0.7 g of omega-3 per day. Due to complications during cancer treatment, 4 patients needed to increase the amount to 90-120 g/day, which is equivalent to a total of 396 calories, 27 g of protein and 0.9 g of omega-3 per day. Also, 2 patients during the intervention reduced the prescribed amount to 30 g, equivalent to a value of 132 calories, 9 g of protein and 0.35 g of omega-3 per day. It is worth mentioning that the characteristic flavor of omega-3 was reported as one of the difficulties in accepting the total intake of the supplement, but when diluted in the recipes proposed in the e-book, the flavor of omega-3 was irrelevant. Another point to be highlighted is that the patients did not follow any type of hypercaloric or hyperprotein diet.

DISCUSSION

Patients with gastrointestinal tract tumors have a high prevalence of malnutrition. This is due to several factors, including reduced appetite, impaired digestion and absorption, increased metabolic demands, and side effects of cancer treatment. Malnutrition can have a significant impact on the patient's overall health and quality of life, as well as on the efficacy and tolerability of cancer treatments[3]. Early

Table 1 – Results obtained (mean ± standard deviation) by 3D computed tomography of the body composition of patients sampled before and after nutritional intervention.

Variables	Pre-intervention (n=12)	Post-intervention (n=12)	P-value	Difference between means (95% CI)	Cohen's d
Muscle area (cm2)	128.8±24.97	127.7±30.31	0.84	1.09 (-10.70 to 12.88)	58
MMI (cm/m^2)	47.7±8.17	47.3±10.18	0.82	0.43 (-3.78 to 4.66)	66
Visceral fat (cm^2)	84±60.87	89±83.86	0.68	-5.72 (-35.43 to 23.98)	-122
Subcutaneous fat (cm^2)	116.1±61.02	119.6±76.3	0.77	-3.57 (-30.42 to 23.27)	-84
Total fat area (cm^2)	200.1±93.08	209.4±133.61	0.68	-9.28 (-58.66 to 40.09)	-199
CC (cm)	33.5±3.24	33.8±3.54	0.59	-0.33 (-1.69 to 1.02)	-156
BMI (kg/m^2)	22.4±2.33	22.5±2.91	0.87	-0.06 (-0.99 to 0.85)	-45

n = sample size; MMI = muscle mass index; CC = calf circumference; BMI = body mass index; 95% CI = 95% confidence interval.

Table 2 – Result of the classification of the Subjective Global Assessment (SGA) in the pre- and post-nutritional intervention period. Percentages in parentheses.

SGA-PPP Category	Pre-intervention (n=12)	Post-intervention (n=12)
A - Well nourished	1 (8.3)	3 (25)
B - Moderately malnourished	10 (83.3)	7 (58.3)
C - Severely malnourished	1 (8.3)	2 (16.7)

n = sample size.

recognition and intervention of malnutrition is crucial to improving the cancer patient journey. It involves a multidisciplinary approach, including a comprehensive nutritional assessment, early identification of nutritional risk factors, and multimodal intervention with appropriate nutritional support, including for symptom and side effect management[1,3].

During the oncological treatment carried out in this study, approximately 67% of the patients presented gastrointestinal symptoms resulting from the treatment and the disease, these factors interfered with the total adherence to the proposed oral nutritional therapy. Other studies[8,9] also indicate a high incidence of these gastrointestinal symptoms resulting from chemotherapy and radiotherapy.

Malnutrition and metabolic disorders, often present in cancer patients, can negatively impact the evolution of the treatment of the disease[10]. However, regarding the nutritional aspects of this study, despite the difficulties faced by patients during oncological treatment associated with the hypercatabolism of the neoplasia, the BMI percentage and nutritional status of the patients remained stable, without statistically significant differences. This means there was no significant weight loss. This is a positive finding, since weight loss and malnutrition are common complications in cancer patients[2]. The fact that the patients in this study were able to maintain their BMI and nutritional status without regressions is a positive result and suggests that the nutritional interventions provided were effective in supporting their nutritional needs.

BMI is a traditional anthropometric tool, but it should not be used alone as a nutritional assessment instrument, as it may impair the diagnosis of malnutrition[11]. In this study, when using SGA as a tool to assess nutritional status, which considers a variety of factors, no statistically significant changes were observed. This result can be seen as positive, since cancer patients with tumors in the gastrointestinal tract tend to develop malnutrition quickly if nutritional intervention is not performed. However, the patients in this study did not show any worsening in nutritional status after the intervention, as indicated by the statistical analysis of the results.

CC is recognized by the Asian Working Group for Sarcopenia 2019 consensus and by the World Health Organization as a marker of muscle mass in older adults. Results from different studies support the usefulness of CC as a surrogate marker for measuring muscle mass[7]. The nutritional intervention used in this study was effective in increasing muscle mass values assessed by CC in most cancer patients when values were analyzed pre- and post-intervention for each patient individually. This finding is significant because sarcopenia and muscle loss are common complications in cancer patients, particularly those undergoing treatment[2].

CC is a simple and noninvasive measurement that can be used to assess muscle mass, and an improvement in this parameter, associated with stabilization of BMI and SGA values, was significantly associated with a lower risk of sarcopenia, corroborating findings from other studies[12]. However, it is worth noting that CC alone may not be sufficient to diagnose sarcopenia or assess muscle mass in all patients, and additional measurements such as those performed in this study may be necessary for a more comprehensive and safe assessment of muscle mass.

Numerous methods have been used in oncological practice to assess nutritional status. Above all, we should highlight the SGA for assessing nutritional status and CT for assessing body composition, methods that are prominent and considered gold standard assessments for this specific population[13]. The main finding determined by CT, if we observe the data before and after nutritional intervention, is the gain in total fat and stabilization of the patients' MMI value. However, when evaluating the MMI result applied to the cutoff point for sarcopenia, we found no significant differences after nutritional intervention. The patients evaluated by this study presented MMI below the defined limit, corroborating with another study[14], which presented that 40.7% of patients undergoing cancer treatment also presented MMI below the limit. In addition, we must consider that as the disease progresses, the greater the weight loss and decrease in the MMI of patients will be[5].

Some findings in the literature indicate that gastrointestinal cancer is one of the types of cancer that has the greatest influence on muscle mass loss in patients[14]. When we observed the MMI data with the SGA from this study, we found an association in the results, where patients who presented low MMI were classified with a diagnosis of moderate or severe malnutrition by the SGA. Similarly, another study[15] evaluated 103 patients with different types of tumors and it was observed that the mean MMI decreased significantly as the nutritional diagnosis by the SGA worsened. Therefore, this data supports the idea that the SGA is a good method for rapid and low-cost nutritional assessment, unlike CT, a method that is difficult to use due to its high cost.

It is important to emphasize that the vast majority of patients included in the study are elderly, who already present a progressive reduction in muscle mass as a physiological and natural process of aging. It is also important to note that there are no specific cutoff points for the Brazilian population and, in the literature, we found numerous cutoff points for defining sarcopenia with CT images[16]. However, we used the cutoff point developed by Prado et al.[5], which is the only one that studied the Canadian oncology population, and which could be relevant to our study. It is also essential to consider factors such as the stage of the disease, the type of oncological treatment and the patient's sex in the definition of sarcopenia. These variables can have an impact on the assessment of muscle mass and overall body composition.

As demonstrated by several studies, patients are muscle depleted at the time of cancer diagnosis and continue to lose muscle throughout the disease course, even in the context of curative disease. Therefore, a nutritional intervention that can halt muscle loss or functional decline can be considered a positive outcome[16]. The data from this study support the use of high-calorie, high-protein supplementation with omega-3 as a promising nutritional intervention for patients with gastrointestinal tract cancer. Despite the numerous complications resulting from cancer treatment and the disease itself, the results of this study, which indicate no significant worsening of nutritional status, are consistent with the findings of other studies[17,18], showing positive results in the nutritional status of cancer patients who used omega-3 supplements.

Omega-3 fatty acids have been shown to suppress systemic inflammatory and oxidative responses, improve patient appetite, and increase weight gain in cachectic cancer patients[18]. This study is also an important finding because chronic inflammation is a known risk factor for cancer and may contribute to the development of cachexia and other complications that rapidly affect nutritional status and overall health outcomes in cancer patients. Taken together, these findings suggest that omega-3 supplementation may be a promising strategy to support the nutritional needs and overall health outcomes of patients with gastrointestinal tract cancer.

The fact that patients did not follow a prescribed high-calorie, high-protein diet and presented treatment-related complications, such as gastrointestinal symptoms that impacted food intake, indicates that the stabilization of nutritional status and body composition was due to the specific interventions used in the study, and not simply to consuming more calories. It also highlights the importance of carefully designing and implementing targeted and comprehensive nutritional interventions, rather than simply increasing calorie intake, in order to effectively support the nutritional needs and overall health outcomes of patients with gastrointestinal cancer.

One limitation of the study was the impossibility of forming a control group, due to its observational nature and the selection of participants by convenience. Thus, the evaluation of the effects of the supplement was done through intra-individual comparisons, that is, each patient was compared with themselves before and after using the product.

CONCLUSION

Based on the information provided, high-calorie and high-protein supplementation, combined with omega-3, when observed in general, had positive effects in the treatment of patients with gastrointestinal tract cancer. These interventions were associated with the maintenance of muscle mass and the attenuation of weight loss, important factors in the overall recovery of the patient during and after cancer treatment. The results of this study suggest that the nutritional intervention protocol used in this research may be a promising approach for future studies and interventions aimed at improving the nutritional status and outcomes of patients with gastrointestinal tract cancer. It is important to note, however, that more research is needed to confirm these findings and determine the optimal nutritional interventions for this population.

Overall, this study provides valuable insights into the benefits of nutritional interventions for cancer patients and highlights the importance of a comprehensive approach to nutritional assessment and treatment.

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Location of the study: Hospital Bruno Born, Lajeado, RS, Brazil.

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