

Nutritional evaluation of surgical patients with gastrointestinal cancer using food supplements

RESUMO | Objetivo: Avaliar a nutrição de pacientes cirúrgicos com neoplasia no trato gastrointestinal em uso de suplemento alimentar. Método: Trata-se de uma revisão sistemática de literatura realizada nas bases de dados Google Scholar, PubMed, Scielo e Web of Science, no período de maio a junho de 2021, sem recorte temporal ou restrição de idioma, através dos descritores: "enteral nutrition e immunenutrition", "cancerpatients e gastriccancerpatients", "preoperative, perioperative e postoperative". Resultados: Foram selecionados 8 estudos, destes, a maioria identificou benefícios na utilização da suplementação em razão da diminuição de células TNF- α , do cortisol e da transferrina, diminuindo o tempo de internação e melhora no estado funcional dos participantes suplementados. Conclusão: Os achados foram positivos, no entanto, houve algumas limitações como a heterogeneidade em abordagens terapêuticas e perda de pacientes durante o estudo, apesar de apresentarem baixo risco de viés, ainda há a necessidade de mais estudos.

Descritores: Suplementos Nutricionais; Neoplasias Gastrointestinais; Oncologia Cirúrgica; Avaliação Nutricional.

ABSTRACT | Objective: To evaluate the nutrition of surgical patients with neoplasia in the gastrointestinal tract using food supplements. Method: This is a systematic literature review carried out in Google Scholar, PubMed, Scielo and Web of Science databases, from May to June 2021, without time frame or language restriction, using the descriptors: "enteral nutrition and immunenutrition", "cancerpatients and gastriccancerpatients", "preoperative, perioperative and postoperative". Results: Eight studies were selected, most of which identified benefits in the use of supplementation due to the decrease in TNF- α cells, cortisol and transferrin, reducing the length of hospital stay and improving the functional status of supplemented participants. Conclusion: The findings were positive, however, there were some limitations such as heterogeneity in therapeutic approaches and loss of patients during the study, despite having a low risk of bias, there is still a need for further studies.

Keywords: Nutritional Supplements; Gastrointestinal Neoplasms; Surgical Oncology; Nutritional Assessment.

RESUMEN | Objetivo: Evaluar la nutrición de pacientes quirúrgicos con neoplasia en el tracto gastrointestinal utilizando suplementos alimenticios. Método: Se trata de una revisión sistemática de la literatura realizada en las bases de datos Google Scholar, PubMed, Scielo y Web of Science, de mayo a junio de 2021, sin franja horaria ni restricción de idioma, utilizando los descriptores: "nutrición enteral e inmunonutrición", "pacientes oncológicos y pacientes con cáncer gástrico", "preoperatorio, perioperatorio y postoperatorio". Resultados: Se seleccionaron ocho estudios, la mayoría de los cuales identificaron beneficios en el uso de la suplementación por la disminución de células TNF- α , cortisol y transferrina, reduciendo la estancia hospitalaria y mejorando el estado funcional de los participantes suplementados. Conclusión: Los hallazgos fueron positivos, sin embargo, hubo algunas limitaciones como la heterogeneidad en los enfoques terapéuticos y la pérdida de pacientes durante el estudio, a pesar de tener un bajo riesgo de sesgo, aún existe la necesidad de realizar más estudios.

Palabras claves: Suplementos Nutricionales; Neoplasias Gastrointestinales; Oncología Quirúrgica; Valoración Nutricional.

Lainny Coelho Rodrigues

Graduate in Nursing. FAMETRO University Center (CEUNI-FAMETRO). Manaus (AM), Brazil.

ORCID: 0000-0003-4294-6630

Ayrton Rogério Nascimento dos Santos

Graduate in Nursing. FAMETRO University Center (CEUNI-FAMETRO). Manaus (AM), Brazil.

ORCID: 0000-0002-2518-5705

Clarissa Souza Lacorte

Graduate in Nursing. FAMETRO University Center (CEUNI-FAMETRO). Manaus (AM), Brazil.

ORCID: 0000-0003-0925-8780

Larissa Adriane dos Santos Mos

Nutritionist. FAMETRO University Center (CEUNI-FAMETRO). Manaus (AM), Brazil.

ORCID: 0000-0001-7739-6312

Felipe Rodolfo Pereira da Silva

Biomedic. Professor, Graduation in Medicine, Federal University of Pará. Postdoctoral fellow, UFPI Postdoctoral Program. Teresina (PI), Brazil.

ORCID: 0000-0001-9224-5571

Graciana de Sousa Lopes

Nurse. Professor, Graduation in Nursing, FAMETRO University Center (CEUNI-FAMETRO). Master in Nursing from UFAM. Manaus (AM), Brazil.

ORCID: 0000-0003-3615-9040

Ana Elis Guimarães Araújo

Nurse, Permanent Nursing Education at the Amazonas Oncology Control Center Foundation. Master in Applied Sciences to Dermatology from the University of the State of Amazonas (UEA). Manaus (AM), Brazil.

ORCID: 0000-0003-0368-1908

Júlia Mônica Marcelino Benevides

Nurse. Professor, Graduation in Nursing from the FAMETRO University Center (CEUNI-FAMETRO). Doctoral student in the Post-Graduation Program in Basic and Applied Immunology at UFAM. Manaus (AM), Brazil.

ORCID: 0000-0002-4410-1431

Recebido em: 11/10/2022

Aprovado em: 12/11/2022

INTRODUÇÃO

According to the International Agency for Research on Cancer (IARC), in a 2018 publication, there were a total of 18 million cases in the world, and in a projection for 2040, it informs that there will be 29 million new cases. In third place of the most incident neoplasms in the world with about 1.8 million cases, it is the most predominant gastrointestinal tract neoplasm. In Brazil, it is estimated that in the three-year period 2020-2022 there will be the occurrence of 450,000 new cases of cancer per year, excluding non-melanoma skin cancer. Among the five most incidents, the colon and rectum are in third place (41 thousand cases) and in fifth place, stomach cancer (21 thousand cases).^{1,2}

Gastrointestinal tract neoplasm (GI) causes metabolic modifications, where a macronutrient such as carbohydrates becomes preferentially used by cancer cells compared to non-cancerous ones. There is also an increase in lipolysis and a reduction in lipogenesis, leading to a decline in their adipose tissue. In addition, there is loss of muscle mass due to the catabolization of protein content, which becomes increased, resulting in negative tissue repair, favoring infectious episodes.³

This factor directly impacts the progression of the disease and the patient's quality of life. About 15% to 50% of patients are sarcopenic, 25 to 80% are anorexic and 10 to 20% of cancer patients die from malnutrition and not from the neoplasm itself, therefore, nutritional therapy should be started before the nutritional status worsens, following the orientation of a diet improved in energy and protein. In surgical patients at risk of malnutrition or malnourished, nutritional support is recommended during the hospital period and after discharge, and those undergoing surgical resection of cancer in the upper gastrointestinal tract should use either oral or enteral immunonutrition, a nutritional supplement enriched with arginine, n-3 fatty acids and nucleotides, which cause a reduction in postoperative complications.^{4,5}

Some studies have identified that the use of nutritional supplements such as immunomodulatory nutrition based on n-3 fatty

acids, nucleotides, glutamine and arginine are causing immune system suppression after surgical stress, and another nutrition alternative is pharmaconutrition that acts on the progress of oral intake.⁶

In view of the above, the following ques-



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tion arose: What are the benefits of dietary supplementation for patients with cancer in the gastrointestinal tract undergoing a surgical procedure? For this reason, the objective of this review was to evaluate the nutrition of surgical patients with neoplasia in the gastrointestinal tract using food supplements.

METHOD

This is a research clipping of the Scientific Initiation Support Program (PAIC) of the Amazonas Oncology Control Center Foundation (FCECON) under CAAE:97561018.7.0000.0004 and opinion nº 4.353.338 financed by the Research Support Foundation of the State of Amazonas (FAPEAM). It followed the PRISMA guidelines that define the correct design of systematic review and meta-analysis studies.⁷ The systematic search was carried out in the Google Scholar, PubMed, Scielo and Web of Science databases, from May to June 2021, without delimitation of publication period, using the combination of the following descriptors: “enteral nutrition and immune nutrition”, “cancer patients and gastric cancer patients”, “preoperative, perioperative and postoperative”. No language restrictions were applied and the references of the collected studies were analyzed to collect potential additional studies.

To be included in this systematic review, studies should meet the following criteria: (1) be an original study and (2) use a supplement enriched with omega 3. Studies with patients diagnosed with other types of cancer outside the gastrointestinal tract, patients with comorbidities such as chronic kidney disease, diabetes or autoimmune diseases, literature review studies or systematic review were excluded.

In the search carried out in the databases, 183 studies were initially identified. With the removal of duplicates, 154 remained, and after going through the eligibility process, 8 articles were selected, according to the methodological process observed through the flowchart (Figure 1).

Data were collected following a standardized form according to: author, year, total number of participants included, cancer diagnosed, supplement used and duration. This form composed the table of characteristics of the included studies.

The Cochrane tool was used to assess the methodological quality of the included stu-

dies in which domains were analyzed regarding the selection, allocation and treatment of data in the studies.

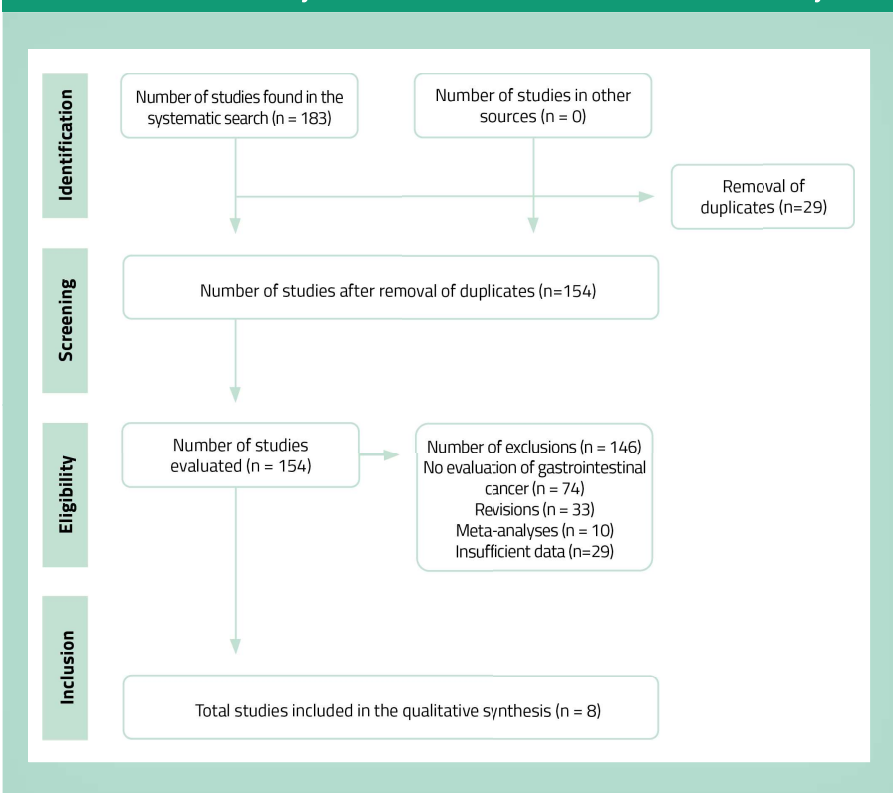
RESULTS

The selected works and their characteristics are shown in Table 1. The studies evaluated a total of 2,172 patients submitted to therapeutic modalities of oral, parenteral or enteral supplementation versus the use of placebo or who did not use supplements or placebo. The studies were published between 2002 and 2016 and addressed gastrointestinal cancer under the diagnosis of: colorectal, stomach, pancreas, esophagus, biliary tract and liver. Of these studies, three were carried out in Italy. 8-10, one in Brazil 11, one in Switzerland 12, one in China 13, one in France 14 and one in Australia. 15

Risk of bias analysis according to the Cochrane tool of the selected trials is described in Figure 2.

After selection, the analysis of the studies was carried out in the axes:

FIGURE 1. Flowchart of the systematic selection of articles included in the study, 2021.



Source: Authors, 2021.

TABLE 1. Characteristics of the studies included in the review according to author/year, participants, supplement used, methodology and considerations, 2021.

Author/Year	Participants	Supplement	Method	Results
Gianotti L. et al., 2002	305 with gastrointestinal CA	Impact ®	Group I – 5d orally; Group II - 5d orally + parenterally in the postoperative period; Group III- did not use.	Significant improvement in groups I and II regarding the use of nutritional therapy, the use of the supplement both preoperatively and perioperatively demonstrate efficacy in addition to reducing side effects. Regarding infections, there were no significant statistical data.
Braga M. et al., 2002	200 with colorectal CA	Impact ® e dieta isoenergética	Group I- 5d orally + postoperative via parenteral; Group II- 5d orally; Group III- 5d orally (isoenergetic diet); Group IV- did not use.	Reduced postoperative infection in supplemented and non-supplemented groups. The supplement showed more inflammatory than nutritional response.
Bozzetti F. et al., 2007	1410 with colorectal, stomach and pancreas CA	Impact ®	Group I - immunomodulatory nutrition (Impact ®); Group II- enteral nutrition; Group III- total parenteral nutrition; Group IV - intravenous fluids, glucose if well nourished and amino acids if poorly nourished.	There was benefit in all nutrition pathways, especially in patients with severe weight loss. Therapies using supplements compared to intravenous fluids also had important outcomes in patients who had not lost >10% weight in recent months. It showed a reduction in infectious complications, suggesting that the nutritional intake modulates the immune system even in conditions of post-surgical immunosuppression.



Giger, U. et al., 2007	46 with gastrointestinal CA	Impact® e Impact Plus Glicina	Group I (Impact®) - 5d orally + 7d postoperatively; Group II (Impact Plus) - 2d orally + 7d postoperatively; Group III (Impact®) - orally 7d only in the postoperative period.	It showed a significant reduction in perioperative inflammation, as well as in postoperative complications compared to group III. The efficiency of both Impact Plus and Impact® in the preoperative period was highlighted.
Marques, D et al., 2013	21 Stomach, Esophagus, Biliary Tracts and Pancreas CA	Placebo em cápsula e Ômega-3 em cápsula	Grupo I (Placebo) - 14d via oral, 2 doses/d Grupo II - (Ômega-3) - 14d via oral 2 doses/d	None of the participants reported adverse reactions or any other symptoms. There was no statistical difference in weight loss between the two groups, however, in group I (70%) the participants lost weight, while in group II (72%) they gained weight, in addition to improvement in serum levels of Transferrin and decrease in CRP and Cortisol levels, which demonstrates better acute phase inflammatory response and stabilized weight loss.
Xu, J. et al., 2006	60 with gastrointestinal CA	Impact® e Nutrição Enteral Padrão	Group I (Placebo) - 14d orally, 2 doses/d, Group II - (Omega-3) - 14d orally 2 doses/day	He observed that there were no significant differences regarding the immunological and nutritional variables between the two groups, however, there was a decrease in postoperative complications, as well as hospitalized days for the group that used the Impact®
Seguin, P. et al., 2016l	35 with liver CA	Impact® e Placebo	Group I - (Impact®) - 3 times a day, 7d preoperatively orally and 3d postoperatively parenterally, Group II - Placebo - 3 times a day, 7d preoperatively orally and 3d postoperatively via parenteral	It showed a small difference in infections and adverse problems, four participants suffered some type of infection and only one who used the Impact® had an infection, however, it is not a statistical difference. It also reports that there was no major recovery in the liver function of the participants.
Barker, L. A. et al., 2013	95 with gastrointestinal CA	Impact®	Group I - (Impact®) - 3 times a day, 5d orally, Group II - No supplementation	It proved to be more positive for malnourished patients, reducing hospitalization time and consequently reducing costs.

Source: Authors, 2021.

type of surgery, division of the control group, nutritional supplement used, period of use of the supplement and clinical outcomes found in the scope.

DISCUSSION

Patients with GI neoplasms are at risk of losing muscle mass due to sarcopenia and cachexia, both of which are frequent manifestations and considered secondary in relation to the mechanical effects of GI neoplasms and are also justified by neuroendocrine changes and the inflammatory process. 16

In this sense, a study carried out in Switzerland demonstrated a lower level of TNF- α in the postoperative period in those who used supplementation compared to those who did not use it, the control group differing from the treatment group by the expressive increase

of this pro-inflammatory cytokine with great statistical significance, knowing that this increase is associated with a negative prognosis. There was also a higher leukocyte elevation in the control group, however, there was no significant discrepancy in values in relation to the other groups. Regarding interleukin, specifically IL-6, it was found to be high in the first moments of the postoperative period in all groups, however, at later times, the groups treated with supplementation obtained values similar to preoperative values, in contrast to the control group that followed with elevated cytokine levels. In addition, the study highlights the attenuation of infectious complications in the postoperative period. 12

Knowing that the development of cancer repeatedly leads to great weight loss, and with the patient's submis-

sion to the stress present in the surgical process when necessary, it precedes a systemic inflammatory response, positively influencing a good prognosis and their immune system. 17

The same was observed in studies in Italy and China when demonstrating the depletion of infectious complications, emphasizing the positive efficiency of the immunomodulator. 9,10,12,13 In this context, nutritional supplements enriched with omega-3 are highlighted because they act in the immunomodulation of the immune system, suppressing significant inflammatory responses in the postoperative period. 16

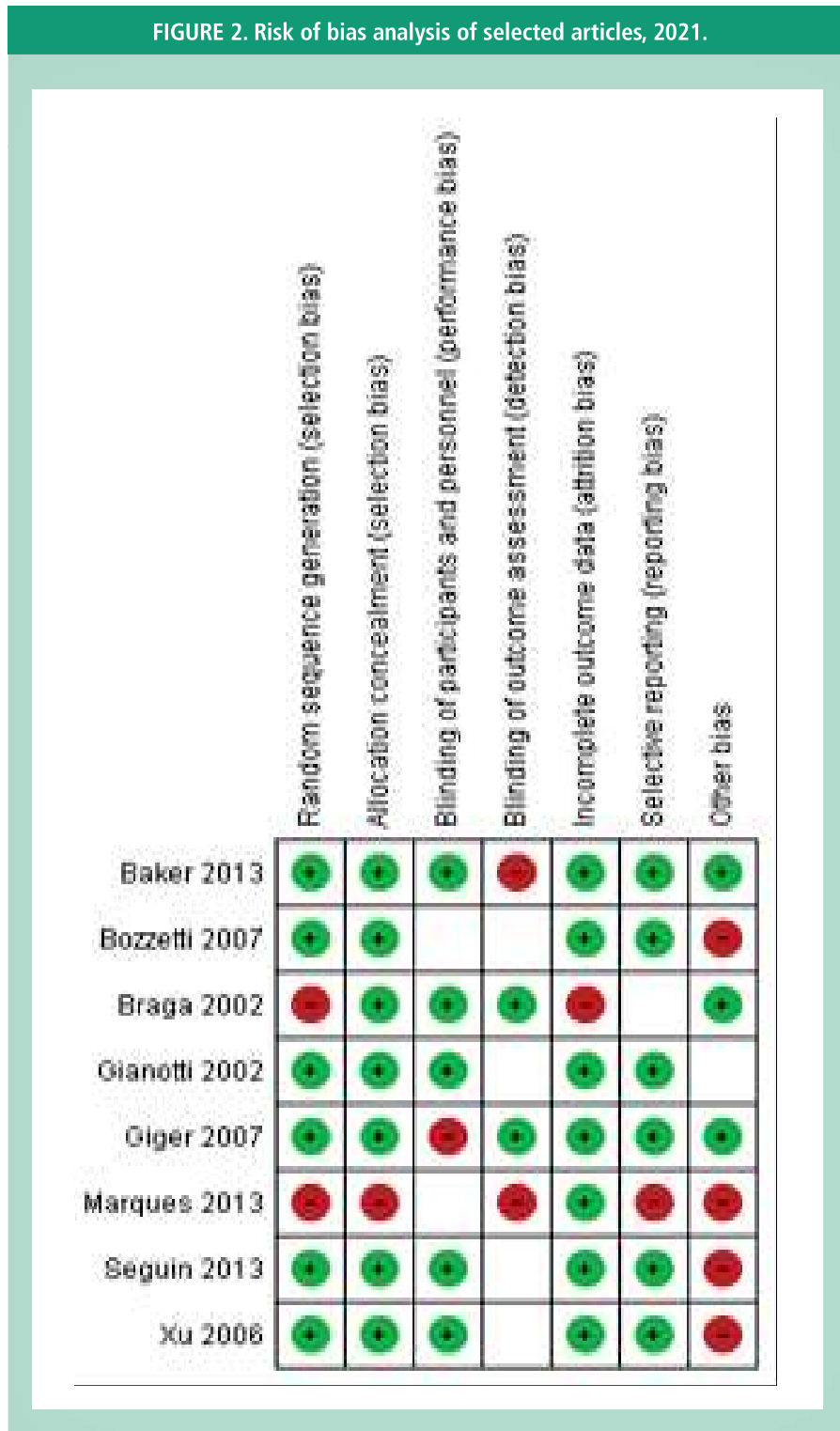
In Brazil, the immunological results were positive to act in the response caused by surgical stress, such as a lower level of C-reactive protein in the group that received supplements in this way, highlighting the possible decrease

in the inflammatory response and metabolic stress, also observed that there was a decrease in cortisol and an increase in transferrin. In addition, it analyzed the level of functional capacity in the participants and demonstrated a considerable increase in the participants who used the enriched omega-3 capsules compared to the others. 12

Regarding weight loss of 10% in the last 6 months, it was shown to be one of the variables in some studies, it is known that this loss makes these patients considered malnourished, so the supplement may have different outcomes in nourished patients, which represents a possible methodological bias within the studies, the explanation for this is seen in a study where they explain that malnourished patients imply in the immune response and need more energy and nitrogen. 9-13 As an example, two studies that worked only with well-nourished patients who had not lost >10% in the last 6 months, efficacy was identified in the groups that used immunonutrition, and the other group showed an increase in biomarkers of liver regeneration, γ -GT and a-FP, but did not result in improvement in liver function. However, in both studies there was no reduction in post-surgical complications when using the supplement. 9,15

Indication of nutritional support must follow criteria that consider the individuality of the patient, nutritional status, disease stage, treatment effects and gastrointestinal function. Due to technological innovations, in the last ten years, there have been great advances in nutritional therapy, which has made it possible to increase its effectiveness and reduce the risks of complications. 16

Therefore, there is a reflection on the use of food supplements as a way to reduce expenses related to gastrointestinal surgeries, considering that post-surgical complications would reduce, and thus, causing a shorter length of



Source: Authors, 2021.

stay in the hospital unit, generating financial benefits for the hospital and for

the patient. Therefore, a reduction of 1.7 days of hospital stay was identified

in those who used the supplement, but it clarifies that despite demonstrating results, it still did not reach statistical calculation, although it showed a decrease in the rates of complications in these participants. The author makes the caveat that the failure to reach the data as expected may be related to the low power of the study, which lasted 26 months due to the slowness in recruiting these patients. 15

Despite the mostly positive developments in the controlled groups, there are still differences found in the studies that need to be clarified, mainly due to the variety of study designs.

CONCLUSION

In fact, the use of omega-3 has been shown to be effective in patients in several studies of malnourished cancer patients, especially at biochemical levels, in addition to improving the lives of these patients, promoting less dependence on other people and reducing hospitalizations. It was observed that in the articles there was an improvement in physical capacity and response in the reduction of complications and length of stay. Patients with a more debilitated nutritional status had better outcomes with the use of supplements and shortening their hospitalization period.

Although these findings show the role of omega-3 as a potential supplement for immunotherapy in GIT

neoplasms, some limitations must be noted. First, the studies were very heterogeneous, both in terms of therapeutic approaches and the methodological design used. According to the limited number of participants included, due to the enormous loss of patients during treatment, influence on the quantification of scientific evidence on this topic. Third, the high methodological heterogeneity of the studies prevented a meta-analytic approach to the data.

Regarding such limitations, the studies showed significant methodological quality in which most of them received a low risk of bias score. However, further studies are needed to validate the results of this systematic review.

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