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REVIEW ARTICLE

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Major considerations of nutrological therapy in cancer patients: a systematic review

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Abstract

Introduction: Oncological malnutrition is a highly prevalent comorbidity in cancer, limiting patients' quality of life. International and national clinical guidelines recommend supportive nutrition and exercise therapy for cancer patients. **Objective:** It was to present the main approaches to nutritional therapy in cancer patients. **Methods:** The present study followed a concise systematic review model (PRISMA). The literary search process was carried out from August to October 2023 and developed based on Web of Science, Scopus, PubMed, Science Direct, Scielo, and Google Scholar, using scientific articles from 2002 to 2023. The low quality of the evidence was attributed to case reports, editorials, and brief communications, according to the GRADE instrument. **Results and Conclusion:** A total of 81 studies were found that were subjected to eligibility analysis and, subsequently, 16 of the 22 final studies were selected. Most studies showed homogeneity in their results, with X^2 =78.4% >50%. Current dietary guidelines for cancer patients fail to address adequate dietary intake of macro- and micronutrients that can improve patients' nutritional status. Clinical studies and meta-analyses have shown that there is an important impact of a personalized and specific diet on patients during and after anti-neoplastic treatment. Most studies indicate that cancer patients should receive a nutritional assessment immediately after diagnosis. You need to maintain a healthy body weight, with a body mass index of 20–24.9, preserving your lean mass and avoiding an increase in fat mass. Therefore, after diagnosing nutritional status, a conservative energy restriction of 500-1,000 kcal/day should be considered. Nutritional therapy should be based on the patient's nutritional status, eating habits, schedule, activities, and cultural preferences. Therefore, adequate dietary consumption of dietary macro and micronutrients rich in β-carotene and vitamins A, E, and C can prevent the deterioration of nutritional status, also improving the quality of life of cancer patients.

Keywords: Cancer. Nutrological therapy. Oncological malnutrition. Quality of life.

Introduction

Malnutrition and cancer cachexia are highly prevalent comorbidities of cancer, limiting the quality of life of patients and being relevant for prognosis **[1,2]**. International and national clinical guidelines recommend supportive nutrition and exercise therapy for cancer patients **[24]**. Data indicate that nutritional and exercise therapy for cancer patients is so far inadequately implemented, with only 59% receiving nutritional therapy as an integral part of oncological treatment, 66.7% having a nutrition specialist/team, and 65.1% routinely undergoing screening for nutritional status. Support for health policy would be important to create the structural, financial, and personnel conditions for the adequate implementation of the guidelines to achieve optimal treatment of cancer patients **[1]**.

In this scenario of nutritional therapy, macronutrients are represented by carbohydrates, proteins, and fats or lipids, are distributed in food, and should be ingested daily to ensure a healthy diet **[5-7]**. Although, as a general rule, a daily percentage of each macronutrient is established, it should be remembered that people perform different activities in different routines and, due to pathologies, may require different dietary and supplement demands **[7]**.

Micronutrients, on the other hand, are represented by vitamins and minerals and are present in a wide variety of foods. Each of these nutrients performs specific functions, essential for the health of our cells and their harmonious functioning. Unlike macronutrients, vitamins and minerals are necessary in small quantities. However, to meet the recommended consumption of these nutrients, they must be supplied through food or supplements daily and from different sources, also depending on the clinical conditions of each individual **[6,7]**.

During the treatment of cancer, many patients present, in addition to weight loss, anorexia, and specific nutrient deficiencies that worsen their clinical and nutritional condition. These patients progress acutely to a condition of severe protein-calorie malnutrition, mainly due to the presence of systemic inflammation. Critically ill cancer patients are in a hypermetabolic and hypercatabolic state, accompanied by proteolysis, lipolysis, and neoglycogenesis. These changes lead to a negative nitrogen balance, which is directly related to increased complications and mortality **[2,5,8]**. Therefore, given this catabolic response, the patient needs to receive an adequate amount of energy and proteins. In the Brazilian Oncology Nutrition Survey, by the José Alencar Gomes da Silva National Cancer Institute (INCA), in 2013, 4,822 cancer patients admitted to 45 Brazilian institutions were evaluated through the subjective global assessment produced by the patient himself. Malnutrition or nutritional risk were present in 2,176 (45.1%) patients studied **[8]**.

Nutritional therapy for critically ill patients aims to maintain homeostasis, improve metabolic and oxidative stress, and reduce complications, length of hospital stay, and mortality. This can be achieved by modulating the immune and inflammatory response **[9,10]**. In this sense, nutritional therapy for the patient was considered adjuvant care, providing exogenous fuel to preserve lean mass during the stress response. In the last three decades, nutritional therapy has the role, in addition to nourishing, of providing nutrients that attenuate the immunoinflammatory response to stress **[11,12]**.

Thus, prescribing adequate nutritional therapy for patients in intensive care is a challenge for the multidisciplinary team. For adequate prescription, the team must consider the results of the screening and nutritional assessment, nutritional needs, choice of administration route, and metabolic capacity that is associated with complications related to critical illness **[12]**. The American Institute for Cancer Research, the American Cancer Society, and the NIH (National Institutes of Health) have published guidelines for oncology nutrition, and patients with inadequate dietary habits need to increase their intake of antioxidants in their diet, with special emphasis on zinc, lycopene, selenium, polyunsaturated fatty acids, and vitamins A, E, and C to reduce the carcinogenic effect that a pro-inflammatory diet can have **[3,7]**.

Therefore, the present study performed a systematic review to present the main approaches to nutritional therapy in cancer patients.

Methods

Study Design

The systematic review rules of the PRISMA Platform were followed. Available at: www.prisma-statement.org/. Accessed on: 10/10/2023.

Data Sources and Search Strategy

The search strategies for this systematic review were based on the Health Science Descriptors (DeCS/MeSH Terms): "Cancer. Nutritional therapy. Oncological malnutrition. Quality of life". The search was carried out from August to October 2023 in the Web of Science, Scopus, PubMed, Science Direct, Scielo, and Google Scholar databases. In addition, a combination of keywords with the Boolean terms "OR", "AND" and the operator "NOT" were used to target the scientific articles of interest.

Study Quality and Risk of Bias

The quality of the studies was based on the GRADE instrument, prioritizing studies with scientifically rigorous methodology, randomized clinical studies, and clinical and/or preclinical studies with significant sample sizes. The risk of bias was analyzed according to the Cochrane instrument.

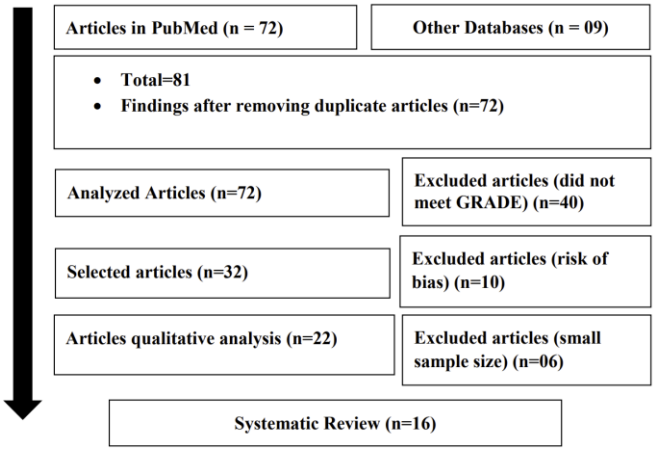
Results and Discussion

Summary of Findings

A total of 81 articles were found. Initially, duplicate articles were excluded. After this process, the abstracts were evaluated and a new exclusion was performed, removing the articles that did not include the topic of this article, resulting in 32 articles. A total of 22 articles were evaluated in full and 16 articles (including 2 websites with guidelines from oncology societies) were included and developed in the present systematic review

study (Figure 1). Considering the Cochrane tool for risk of bias, the overall assessment resulted in 11 studies with a high risk of bias and 28 studies that did not meet GRADE. Most studies presented homogeneity in their results, with X^2 =78.4% >50%.

Figure 1. Flowchart - Article selection process.



Source: Own authorship.

Nutritional Therapy and Oncology

Current dietary guidelines for breast cancer patients fail to address adequate dietary intake of macro and micronutrients that can improve patients' nutritional status **[2-4]**. Thus, one study showed that breast cancer patients should receive a nutritional assessment immediately after diagnosis. In addition, they should be encouraged to seek and maintain a healthy body weight, preserving their lean mass and avoiding an increase in fat mass. Therefore, after the diagnosis of nutritional status, a conservative energy restriction of 500-1000 kcal/day could be considered in the dietary intervention **[8,12]**.

In this context and in a broader way, specifications in nutritional therapy should be based on the patient's nutritional status, eating habits, schedules, activities, and cultural preferences. Daily energy intake in cancer patients should be distributed as follows: <30% fat/d (mainly monounsaturated and polyunsaturated fatty acids), approximately 55% carbohydrates (mainly whole grain foods such as oats, brown rice, and fruits), and 1.2–1.5 g protein/kg/day to avoid sarcopenic obesity. The results suggest that 5–9 servings/day of fruits (∼ 150 g/serving) and vegetables (∼75 g/serving) should be encouraged. Furthermore, garlic and cruciferous vegetables should also be part of nutritional therapy. Adequate dietary intake of food macro- and micronutrients rich in β-carotene and vitamins A, E, and C can prevent deterioration of oncological nutritional status and improve their general health and prognosis **[13]**.

Several studies report that most cancer patients have an inadequate diet, since their intake of fruits, legumes, green vegetables, and orange vegetables, as well as green tea, decreases, meaning that they do not ingest calcium, iron, phosphorus, magnesium, niacin, riboflavin, thiamine, vitamin B-6, vitamin C, and zinc. Thus, a personalized dietary nutritional intervention that controls energy intake within an acceptable range of macronutrient distribution and that promotes daily consumption of fruits and vegetables will set the standard for nutritional diet therapy **[4,13]**.

Due to the lack of specific nutritional guidelines, the American Cancer Society suggests a nutritional approach that considers the guidelines published in 2007 by NIH in the United States. These guidelines provide more specific recommendations on nutrients (intake of fat, carbohydrates, fiber, cholesterol, etc.) for cancer patients **[7]**.

Also, for weight management, the American Cancer Society recommends a healthy low-fat diet (<30% of total energy) with a strong base of fruits and vegetables (5–9 servings/d) and encourages physical activity **[7]**. A multicenter study reported that only 30–48% of these newly diagnosed patients made positive changes in their dietary habits. These changes include increasing fruit and vegetable consumption and reducing fat and simple sugar consumption. However, almost half of them do not make these positive lifestyle changes **[13]**.

Studies have concluded that cancer patients should consume 5–9 servings/d of fruits (150 g/serving) and vegetables (75 g/serving) to ensure sufficient dietary intake of antioxidants and fiber. Fruits and vegetables should be predominantly those rich in β-carotene and vitamins A, E, and C, as they have been associated with beneficial changes in anthropometric, metabolic, inflammatory, and DNA methylation markers. There is evidence that dietary intake of foods rich in polyphenols, such as onions, broccoli, and apples (whole), among others, should be encouraged to improve cancer outcomes **[13]**.

It is suggested that animal protein sources, such as meat, eggs, and low-fat dairy products, be consumed in moderation (1 to 2 times per week), and fish, poultry, turkey, and pork loin should be chosen as better options due to their low-fat content. Studies in elderly individuals have demonstrated the effectiveness of maintaining fat-free mass and reducing the risk of sarcopenic fat, ensuring the consumption of 1.2-1.5 g of protein/kg/day **[13]**.

Nutritional recommendations for critically ill cancer patients range from around 25 to 30 kcal/kg of current weight/day and the amount of protein between 1.5 and 2.0 g/kg of current weight/day. In the acute phase of the response to injury, the need is between 20 and 25 kcal/kg of current weight/day. For critically obese patients with a body mass index (BMI) between 30 and

50 kg/m², the caloric intake should be between 11 and 14 kcal/kg of current weight/day. For obese patients with a BMI greater than 50 kg/m², the caloric intake is 22 to 25 kcal/kg of ideal weight/day **[2,4,8]**.

Most critically ill patients require high-protein diets. This macronutrient is the most important fuel used in the metabolic response to stress. In this context, the protein intake is increased to between 1.2 and 2.0 g/kg of current weight/day. On average, the recommendation is around 1.5 g/kg of current weight/day. For critically ill obese cancer patients with a BMI between 30 and 40 kg/m², the protein intake should be 2.0 g/kg of ideal weight/day and 2.5 g/kg of ideal weight/day for patients with a BMI greater than or equal to 40 (Tables 1 and 2) **[8]**.

Table 1. Caloric and protein guidelines for cancer patients.

Questions	Answers
What method should be used to estimate caloric needs?	Indirect calorimetry (IC) - whenever possible In the absence of IC, use a simple formula to estimate kcal/kg of current weight/day In the presence of edema or anasarca, use dry or usual weight
What is the calorie requirement?	Acute phase of treatment or in the presence of sepsis: 20 to 25 kcal/kg of current weight/day Recovery phase: 25 to 30 kcal/kg of current weight/day Critically obese with: - BMI of 30 to 50 kg/m²: 11 to 14 kcal/kg of current weight/day - BMI > 50 kg/m²: 22 to 25 kcal/kg of ideal weight/day
What are the protein recommendations?	From 1.5 to 2.0 g/kg of current weight/day. Critically obese with: - BMI of 30 to 40 kg/m²: 2.0 g/kg of ideal weight/day - BMI ≥ 40 kg/m²: 2.5 g/kg of ideal weight/day
What are the water recommendations?	From 30 to 35 ml/kg of current weight/day

Source: Adapted **[8]**.

Table 2. Macronutrient consumption percentage guideline.

Macronutrients	Reference (DRI**)
Carbohydrate	45 – 65% of TEV*
Protein	10 – 35% of TEV
Lipid	20 – 35% of TEV

*TEV=Total Energy Value. **DRI=Dietary Reference Intakes.
Source: Adapted **[8]**.

Evidence suggests that vitamin and mineral deficiencies can cause damage to the cell's genetic material, as shown in Table 3.

Table 3. Main effects of micronutrients.

Vitamins and minerals	Antineoplastic effect
• Decreased B-12, B-6, C and E; folic acid; niacin; iron; and zinc	• Mimic the effect of radiation on DNA, causing oxidative damage
• Vitamin A and retinoids	• Inhibition of carcinogenesis
• Garlic and cruciferous vegetables (3,39-diindolylmethane).	• Antiproliferative and antioxidant activity in breast cancer cells.

Source: Adapted **[12]**.

Furthermore, selenium and polysaccharide combinations can be identified in three forms natural selenium polysaccharides, synthetic selenium polysaccharides, and polysaccharidedecorated selenium nanoparticles. Studies have shown that these three combinations generally exhibit better bioactivities, including immunomodulation, antitumor, antioxidation, and glucose regulation, than those of selenium or polysaccharides alone. Although they have not yet been developed as new drugs for clinical trials, the results of previous studies have already shown their therapeutic potential for the future **[14]**. In addition, vitamin D3 supplementation has a beneficial effect on cancer patients. One study investigated the effect of vitamin D3 consumption on redox and metal homeostasis in prostate cancer. Forty-three volunteers were involved in the study. Patients were divided into 5 groups: (A) patient control (N=8), (B) patient control with vitamin D3 treatment (N=9), (C) high-risk prostate cancer group (N=6), (D) highrisk prostate cancer group with vitamin D3 treatment (N=8), and (E) vitamin D3-treated cancer group with androgen deprivation therapy (N=11). Vitamin D3 treatment caused differences in metal and redox homeostasis in both patient control and cancer groups. Iron, chromium, and lead concentrations were significantly increased in erythrocytes of prostate cancer patients. It appears that vitamin D3 helps to balance redox homeostasis which could positively affect cancer outcome **[15]**.

Finally, one study evaluated dietary intake at different times of the chemotherapy cycle. Fifty-five ovarian cancer patients receiving at least two cycles of chemotherapy were considered eligible for this study, of which 41 participants completed the study. Anthropometric measurements and Subjective Global Assessment were used to estimate nutritional status. Dietary intake was assessed by 3-day food records: 3 days before, on the day of, and the day after chemotherapy. Mean energy intake was lowest on the day of chemotherapy and highest 3 days before treatment (mean difference, 413.8 kcal; $p<0.001$). Similarly, some vitamins and macro- and micronutrients (K, Ca, vitamin D, folate, vitamin C) did not reach 50% of the recommended doses. When dividing patients into

BMI (body mass index, kg/m2) categories, energy intake per kilogram of body weight in normal-weight patients was statistically higher than that in overweight and obese individuals (23.6 vs. 20.9 vs. 12.3 kcal, respectively; p=0.0015). Similarly, statistically significant differences were observed for fat intake (0.80 vs 0.69 vs 0.39 g, p = 0.0283) and carbohydrate intake (3.52 vs 3.05 vs 1.71 g, p = 0.0004). Dietary intake varied across the chemotherapy cycle, with the lowest intake on the day of cytotoxic treatment and the highest before the next chemotherapy **[16]**.

Conclusion

Current dietary guidelines for cancer patients fail to address adequate dietary intake of macro- and micronutrients that can improve patients' nutritional status. Clinical studies and meta-analyses have shown that there is an important impact of personalized and specific diets on patients during and after antineoplastic treatment. Most studies indicate that cancer patients should receive a nutritional assessment immediately after diagnosis. It is necessary to maintain a healthy body weight, with a body mass index of 20-24.9, preserving lean mass and avoiding an increase in fat mass. Therefore, after the diagnosis of nutritional status, a conservative energy restriction of 500-1,000 kcal/day should be considered. Nutritional therapy should be based on the nutritional status, eating habits, schedule, activities, and cultural preferences of the patients. Therefore, adequate dietary intake of food macro- and micronutrients rich in β-carotene and vitamins A, E, and C can prevent the deterioration of nutritional status, also improving the quality of life of cancer patients.

CRediT

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