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THE EFFECT OF NUTRITIONAL INTERVENTIONS TO IMPROVE THE NUTRITIONAL STATUS OF CANCER PATIENTS UNDERGOING CHEMOTHERAPY

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ABSTRACT

Cancer is a catabolic inflammatory disease that causes patients to experience frequent weight loss, or even cachexia in severe cases. Malnutrition in cancer patients impairs quality of life and therapeutic response, further leading to a poor prognosis. This study aims to determine various types of nutritional interventions that can improve the nutritional status of cancer patients undergoing chemotherapy. The research method used is a systematic review through electronic databases and websites, namely PubMed, Scopus, ProQuest, and MedLine. The keywords used for the search were "Nutrition Intervention" AND "Nutritional Status" AND "Cancer patients" OR "Chemotherapy patient". The search for supporting articles was limited to the years 2015-2023, resulting in the identification of 953 articles. After identification, screening, and extraction according to the inclusion and exclusion criteria, 12 articles were included. The research results showed that from 12 research articles, it was found that providing nutritional interventions could be in the form of oral nutritional supplements, omega 3 supplements, as well as other supplements such as propolis, broccoli supplements, and additional parenteral nutrition at home. Providing this nutritional intervention can improve the nutritional status of cancer patients undergoing chemotherapy.

Keywords: cancer patients; chemotherapy patients; nutritional intervention; nutritional status

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INTRODUCTION

Cancer is a disease characterized by the growth of abnormal cells beyond normal limits, which can then invade adjacent parts of the body and/or spread to other organs (WHO, 2018). The Global Burden of Cancer Study (Globocan) by WHO recorded that the total cancer cases in Indonesia in 2020 reached 396,914 cases with a total death toll of 234,511 cases (Handayani, 2022). Chemotherapy is one of the effective therapies in the management of cancer. Repeated chemotherapy can cause various side effects, such as changes in nutritional status (Dewi et al., 2020). Cancer is a catabolic inflammatory disease that causes patients to often experience weight loss, or even cachexia in severe cases. Malnutrition in cancer patients disrupts the quality of life and therapeutic response, which subsequently leads to a poor prognosis. Active screening and nutritional assessment using valid tools are essential for rapid and appropriate nutritional interventions (Kim, 2019).

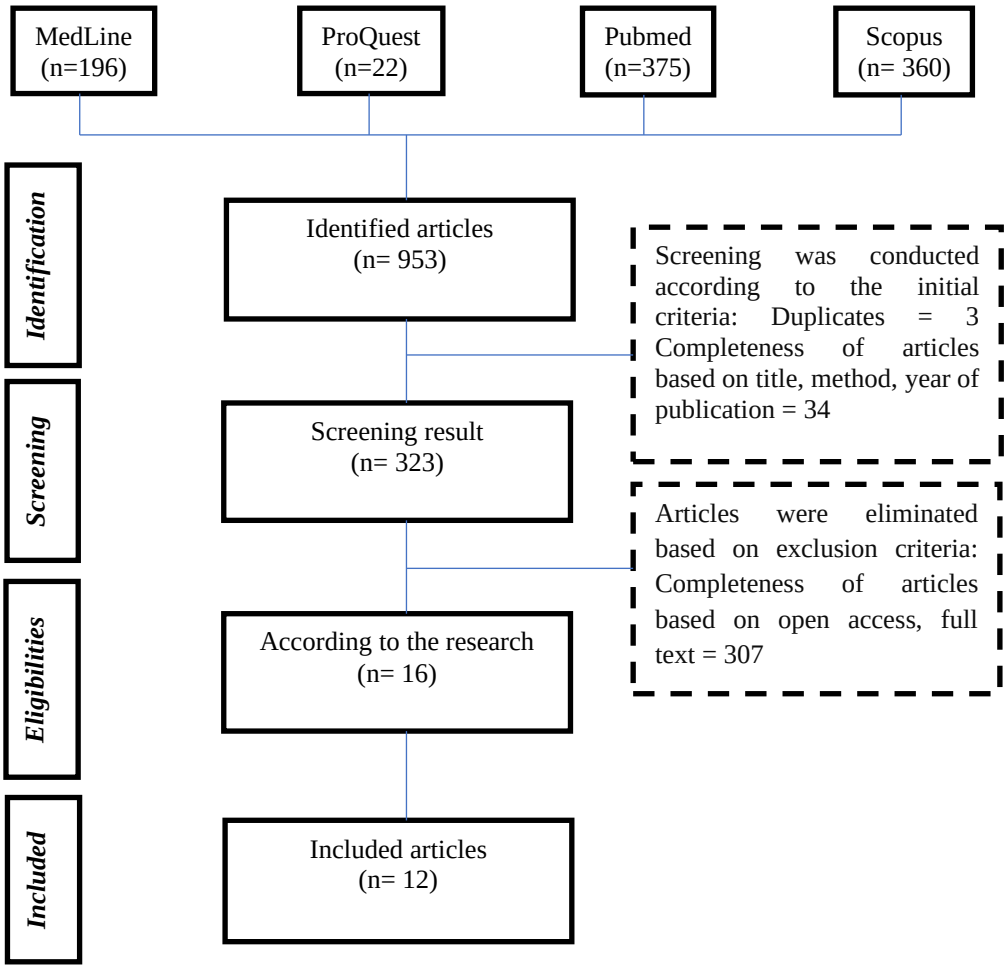
According to Dewi et al. (2020), there is a significant strong negative relationship between the frequency of chemotherapy and the nutritional status of cancer patients, indicating that the more frequent the chemotherapy, the lower the nutritional status of the patients, and vice

versa. A high prevalence of malnutrition and many contributing factors have been identified among elderly cancer patients receiving chemotherapy. Therefore, it is recommended to continuously screen for malnutrition throughout the chemotherapy program with special attention to contributing factors (Abd Allah et al., 2020). Malnutrition is a common problem in cancer patients. It impacts all aspects of patients' lives, such as increased risk of infection, treatment toxicity, hospitalization, and healthcare costs (Muhamed et al., 2022). Integrated care, including palliative care, nutritional therapy, and psychotherapy, can improve the prognosis of patients with advanced gastric adenocarcinoma (Sugiyama, 2023).

A systematic review conducted by Cintoni et al. (2023) on pancreatic cancer patients during chemotherapy does not allow for drawing definitive conclusions. However, nutritional support in pancreatic cancer patients is suggested to enhance oncology care. Further well-designed prospective research is needed to identify the real impact of nutritional support and to determine reliable ways to improve the nutritional status of cancer patients during chemotherapy. The aim of this study is to determine the effect of nutritional intervention on the nutritional status of cancer patients undergoing chemotherapy.

METHOD

This study uses a systematic review design with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) method. The strategy for searching articles/journals uses relevant databases to the research topic, such as Medline, PubMed, ProQuest, and Scopus. The keywords used for the search are "Nutrition Intervention" AND "Nutritional Status" AND "Cancer patients" OR "Chemotherapy patient," with supporting article searches limited to the years 2015-2023. In principle, this systematic review is a research method conducted by summarizing the results of primary research articles to present more comprehensive and balanced data. The selection of articles involves analysis and synthesis based on inclusion and exclusion criteria. The inclusion criteria for selecting articles are cancer patient populations, English language, and publication type being full-text articles and academic journals. The article search was conducted in November 2023. The stages involved in the creation of this article are as follows: 1) Identifying the field of interest related to the topic; 2) Formulating clinical questions based on the PICO framework; 3) Determining inclusion and exclusion criteria before conducting the literature search; 4) Conducting a literature search using the specified keywords and inclusion and exclusion criteria; 5) Extracting and analyzing data; 6) Identifying results.



Picture 1. PRISMA Diagram

RESULTS

Table 1.
Article Analysis

Journal Identified	Research Method	Research Result
Qin et al, China (2021) The Effect of Nutrition Intervention With Oral Nutritional Supplements on Ovarian Cancer Patients Undergoing Chemotherapy	*Single-blinded randomized controlled trial*	This study shows that oral nutritional supplements can significantly reduce the risk of malnutrition in ovarian cancer patients undergoing chemotherapy.
Kimet al, Korea (2019) The Effect of Nutrition Intervention with Oral Nutritional Supplements on Pancreatic and Bile Duct Cancer Patients Undergoing Chemotherapy	*Prospective study, randomized controlled trial*	Oral nutritional supplements can improve nutritional status by increasing fat mass and/or maintaining body composition in pancreatic and bile duct cancer patients undergoing chemotherapy, especially in the first cycle, and reduce fatigue symptoms.
Haidari et al, Iran (2020) Randomized Study of the Effect of Vitamin D and Omega-3 Fatty Acids Cosupplementation as Adjuvant Chemotherapy on Inflammation and Nutritional Status in Colorectal Cancer Patients	*Randomized controlled trial*	The co-supplementation of vitamin D3 plus omega-3 fatty acids in colorectal cancer patients has a beneficial impact on inflammation and nutritional status.

Journal Identified	Research Method	Research Result
Davoodi et al, Iran (2022) Oral Propolis, Nutritional Status and Quality of Life with Chemotherapy for Breast Cancer: A Randomized, Double-Blind Clinical Trial	*A randomized, double-blind clinical trial*	Propolis is suggested as an adequate and safe therapy option to improve nutritional status and quality of life in breast cancer patients diagnosed with receiving chemotherapy.
Lozanovski et al, Jerman (2019) Broccoli sprout supplementation in patients with advanced pancreatic cancer is difficult despite positive effects—results from the POUDER pilot study	*Monocentric, prospective, placebo-controlled, clinical pilot Study*	A non-significant statistical value (p=0.291) was obtained on day 180; however, knowledge about feasibility serves as the basis for developing new drugs.
Abe et al, Jepang (2022) Effects of an enteral nutrient-rich therapy with omega-3 fatty acids in patients with unresectable or recurrent biliary tract cancer or pancreatic cancer during chemotherapy: a case–control study	*A case–control study*	Nutritional therapy rich in Omega-3 fatty acids for pancreatic and bile duct cancer patients undergoing chemotherapy due to inoperability or post-relapse, increases muscle mass without significant side effects.
Akita et al, Jepang (2019) The utility of nutritional supportive care with an eicosapentaenoic acid (EPA)-enriched nutrition agent during pre-operative chemoradiotherapy for pancreatic cancer: Prospective randomized control study	*Randomized controlled trial*	Enriched EPA intake has the potential to improve the nutritional status of pancreatic cancer patients receiving neoadjuvant chemoradiation, but it is difficult for many patients to consume it due to its unpleasant taste.
Mal et al, Jerman (2020) Supplemental home parenteral nutrition improved nutrition status with comparable quality of life in malnourished unresectable/metastatic gastric cancer receiving salvage chemotherapy	*Prospective observational study*	The provision of additional home parenteral nutrition has a positive impact on the nutritional status and quality of life of patients with malnutrition and incurable gastrointestinal cancer shortly after starting treatment.
Gui et al, Spanyol (2023) Effects of omega-3 fatty acid supplementation on nutritional status and inflammatory response in patients with stage II-III NSCLC undergoing postoperative chemotherapy: a double-blind randomized controlled trial.	*A double-blind randomized controlled trial.*	Supplementation of omega-3 fatty acids improves nutritional status and reduces chronic inflammatory response in stage II-III non-small cell lung cancer patients undergoing post-operative chemotherapy.
Jiang et al, China (2018) Benefits of Oral Nutritional Supplements in Patients with Locally Advanced Nasopharyngeal Cancer during Concurrent Chemoradiotherapy: An Exploratory Prospective Randomized Trial	*An exploratory prospective randomized trial*	ONS (Oral Nutritional Supplements) have beneficial outcomes in terms of reducing weight loss, minimizing BMI decrease, and increasing protein intake in locally advanced head and neck cancer patients during chemoradiotherapy.
Aredes et al., Brazil, 2019 Efficacy of omega-3 supplementation on nutritional status, skeletal muscle, and chemoradiotherapy toxicity in cervical cancer patients: A randomized, triple-blind, clinical trial conducted in a middle-income country	*A triple-blind, placebo-controlled, Randomized Controlled Trial (RCT)*	The research findings indicate that omega-3 supplementation is effective in maintaining nutritional status, skeletal muscle quality, and reducing chemoradiotherapy symptoms in women with cervical cancer.
Torricelli et al, Italia, 2020 The oral nutritional supplement prevents weight loss and reduces side effects in patients in advanced lung cancer chemotherapy	*Randomized Controlled Trial*	Early intensive nutritional intervention with Texidrfolico® oral supplements during chemotherapy in NSCLC patients prevents weight loss and benefits their quality of life.

Characteristics of Respondents

From the analysis of 12 journals, the characteristics of the respondents obtained are adult cancer patients undergoing chemotherapy, diagnosed with ovarian cancer, pancreatic cancer, head and neck cancer (HNC), lung cancer, colorectal cancer, cervical cancer, breast cancer, and prostate cancer.

Types of Nutritional Interventions

Types of Nutritional Interventions Research by Qin et al. (2021) shows that oral nutritional supplements can significantly reduce the risk of malnutrition in ovarian cancer patients undergoing chemotherapy. Oral nutritional supplements can improve nutritional status by increasing fat mass and/or maintaining body composition in pancreatic and biliary tract cancer patients undergoing chemotherapy, especially in the first cycle, and reducing fatigue symptoms (Kim et al., 2019). Oral nutritional supplements have beneficial outcomes in terms of reducing weight loss, minimizing BMI decrease, and increasing protein intake in locally advanced head and neck cancer patients during chemoradiotherapy (Jiang et al., 2018). Early intensive nutritional intervention with oral Texidrofolico supplements during chemotherapy in NSCLC patients prevents weight loss and benefits their quality of life (Torricelli et al., 2020). Co-supplementation of vitamin D3 plus omega-3 fatty acids in colorectal cancer patients has a beneficial impact on inflammation and nutritional status (Haidari et al., 2020). Nutritional therapy rich in Omega-3 fatty acids for pancreatic and biliary tract cancer patients undergoing chemotherapy due to inoperability or post-relapse increases muscle mass without significant side effects (Abe et al., 2022). Supplementation of omega-3 fatty acids improves nutritional status and reduces chronic inflammatory response in stage II-III non-small cell lung cancer patients undergoing post-operative chemotherapy (Gui et al., 2023). Research by Aredes et al. (2019) shows that omega-3 supplementation is effective in maintaining nutritional status, skeletal muscle quality, and reducing chemoradiotherapy symptoms in women with cervical cancer. Propolis is suggested as an adequate and safe therapy option to improve nutritional status and quality of life in breast cancer patients diagnosed with receiving chemotherapy (Davoodi et al., 2022). Broccoli supplementation in prostate cancer patients undergoing chemotherapy showed a lower average death rate in the treatment group during the first 6 months after consumption, and Kaplan-Meier analysis indicated a higher survival rate (Lozanovski et al., 2019). Intake of Eicosapentaenoic Acid (EPA)-enriched supplements potentially improves the nutritional status of pancreatic cancer patients receiving neoadjuvant chemoradiation, but it is difficult for many patients to consume it due to its unpleasant taste (Akita et al., 2019). Additional home parenteral nutrition has a positive impact on the nutritional status and quality of life of patients with malnutrition and incurable gastrointestinal cancer shortly after starting treatment (Mal et al., 2020).

DISCUSSION

Cancer is a complex disease caused by various interactions between genes and the environment, and is considered one of the leading causes of death worldwide. Metabolic and nutritional changes can affect the survival and recovery of cancer patients (Ravasco, 2019). This intensive treatment regimen increases acute toxicity, which can negatively impact the nutritional status of patients (Miao et al., 2023). Cancer treatment with chemotherapy disrupts the digestive system, leading to symptoms such as nausea, vomiting, mucositis, diarrhea, and constipation, which can decrease food intake. Malnutrition in cancer patients is a common complication that will negatively impact therapy outcomes, as well as increase morbidity and mortality (Santosa et al., 2019). The human body cannot maintain normal physiology, biochemical function, immune function, growth and development, metabolism, repair, and other vital activities without nutritional support (Qin et al., 2021). Nutritional intervention

support is essential to support the nutritional status of cancer patients receiving chemotherapy. Interventions are needed to improve the detection of conditions and increase awareness and nutritional status of affected patients (Alsaleh et al., 2021). Preoperative nutritional status in head and neck cancer patients affects swallowing function and post-resection nutritional status. Specifically, dysphagia and malnutrition easily occur, up to 2 months after surgery, indicating the importance of preoperative nutrition management and rehabilitation (Sakuramoto et al., 2021). From the 12 journals discussed, it was found that nutritional intervention can be in the form of: oral nutritional supplements, omega-3 supplements, and other supplements such as: propolis, broccoli supplements, and additional home parenteral nutrition.

Oral nutritionals supplements

Oral Nutritional Supplements The principle of nutrition during anticancer therapy should mainly consider light and low-fat foods, exemption from foods containing lactose and gluten in certain cases, or the introduction of special food products such as oral nutritional supplements (Lewandowska et al., 2022). Oral nutritional supplements are an important, effective, and non-invasive intervention for patients who can consume them. Oral nutritional supplements can significantly increase the nutritional risk of ovarian cancer patients undergoing chemotherapy compared to the control group, and that oral nutritional supplements have advantages because they are simple, easy to administer, and physiologically appropriate and should be the first choice for enteral nutrition therapy (Qin et al., 2021). Oral nutritional supplements can increase fat mass in pancreatic and biliary tract cancer patients undergoing chemotherapy along with an increase in nutritional status scores and fatigue symptom scores on the EORTC QLQ-C30. Body fat reduction in cachexia patients is caused by abnormal enzymatic activation (due to cachexia) that decreases lipogenesis while increasing lipolysis. When about 80% of body fat is depleted, total body weight decreases by 30%, leading to death. In progressive cancer patients, higher rates of fat mass reduction result in a significant decrease in survival rates (Kim et al., 2019).

Oral nutritional supplements are an important treatment strategy, which can provide high amounts of protein and calories, especially in head and neck cancer patients who have difficulty meeting their energy needs due to local tumor factors or adverse effects of anticancer treatment. Since invasive nutritional support methods such as nasogastric tube and percutaneous endoscopic gastrostomy are rarely used in HNC patients, this study provides evidence that oral nutritional supplements are a relatively comfortable and economical nutritional support, which can be beneficial for HNC patients (Jiang et al., 2018). Tumors release high levels of polyamines, which are released into the extracellular environment and stimulate late cell proliferation. Polyamines are small organic cations that are important for normal cell growth and eukaryotic development. Under physiological conditions, intracellular polyamine concentrations are regulated by a series of biosynthetic and catabolic enzymes. This tight metabolic regulation changes with tumor growth; in fact, in many tumors, plasma polyamine concentrations significantly increase. It has been observed that treatment with Texidrofolico, in patients undergoing chemotherapy, has significantly reduced plasma polyamine levels. The components of Texidrofolico are vitamin B and folic acid found in large amounts (Torricelli et al., 2020).

Inflammation plays a crucial role in the development, invasion, metastasis, chemoresistance, and radioresistance of colorectal cancer. Therefore, many studies have been conducted with the aim of developing new anti-inflammatory therapy approaches to suppress the synthesis or function of these factors, especially through food supplements such as vitamin D and omega-3

fatty acids. Inflammation, an inappropriate immunological activity, is a common feature of cancer. The presence and magnitude of chronic systemic inflammatory response can lead to progressive malnutrition. Oral supplementation of various fatty acids alters human immune cells and modifies immune behavior and responses, such as its inflammatory components (Haidari et al., 2020).

Omega-3 fatty acids increase skeletal muscle mass and improve the severity of sarcopenia. When omega-3 fatty acids are given to patients with lung, gastric, colorectal, rectal, pancreatic, head and neck, and biliary tract cancers, their body weight, blood test data (nutrition index and neutrophilia), and quality of life (QOL) scores improve, indicating that omega-3 fatty acids have therapeutic effects on cancer cachexia (Abe et al., 2022). Patients undergoing an omega-3 PUFA-enriched diet experience a dramatic reduction in albumin loss, indicating that omega-3 PUFA contributes to the postoperative nutritional recovery of patients (Gui et al., 2023). Omega-3 suppresses lipogenesis, reduces the deposition of free fatty acids in muscles, and stimulates their oxidation. Supplementation with omega-3 significantly reduces fat content in skeletal muscles after anticancer treatment. Omega-3 supplementation results in weight maintenance and improvement of symptoms affecting nutritional status (Aredes et al., 2019).

Other Supplements

Food supplements containing antioxidants can reduce the toxicity of chemotherapy drugs by reacting and interacting with free radicals and reducing chemotherapy complications. Propolis, rich in flavonoids, contains resinous substances collected by bees from plant extracts and used to make and protect the nest after mixing with wax. Propolis is used in traditional medicine worldwide, and its efficacy as an anti-inflammatory, antioxidant, immune activator, antiviral, antibacterial, and anticancer agent is well-known. Propolis has been considered for several biological functions, including anti-tumor activity, DNA protection, free radicals, and immune system stimulation, as a nutritional supplement in cancer treatment (Davoodi et al., 2022).

Routine consumption of cruciferous vegetables such as broccoli, cabbage, cauliflower, spinach, and radishes is associated with a decrease in cancer incidence. Broccoli supplementation in prostate cancer patients undergoing chemotherapy showed a lower average death rate in the treatment group during the first 6 months after consumption and showed a higher survival rate (Lozanovski et al., 2019). Adopting a higher quality diet and adequate nutritional status are associated with better prognosis for breast cancer patients, and chemotherapy can negatively affect these factors; meal frequency is a modifiable dietary factor relevant to research (Lima et al., 2020).

Parenteral nutrition administration is a solution for patients whose enteral nutrition does not meet their daily nutritional needs. For patients with inoperable or metastatic gastric cancer, home parenteral nutrition supplementation should be considered due to inadequate food intake and prolonged anticancer therapy. Home parenteral nutrition reduces inpatient costs and hospital finances and provides additional time for patients to be cared for in a familiar home environment. For appropriately selected advanced or terminal cancer patients in the context of dysfunctional bowel or malignant bowel obstruction, home parenteral nutrition, as part of palliative care, can also prevent death from starvation and dehydration (Mal et al., 2020). Parenteral nutrition is a complex therapy that should be used wisely when indicated. However, this only covers one part of the multimodal therapy strategy for cancer patients,

including psychological support, symptom management, anticancer therapy, and physical activity (Plyta et al., 2020).

CONCLUSION

Repeated chemotherapy can cause various side effects such as changes in nutritional status. The human body cannot maintain normal physiology, biochemical function and immune response, growth and development, metabolism, repair, and other vital activities without nutritional support. Nutritional intervention support is highly necessary to support the nutritional status of cancer patients undergoing chemotherapy. From the 12 journals discussed, it was found that nutritional intervention can take the form of: oral nutritional supplements, omega-3 supplements, as well as other supplements such as propolis, broccoli supplements, and additional home parenteral nutrition. Providing such nutritional interventions can improve the nutritional status of cancer patients undergoing chemotherapy.

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