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REVIEW ARTICLE

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Palliative medicine and nutritional therapy in critically ill oncological patients: a systematic review

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Abstract

Introduction: In nutritional therapies, appropriate or precise nutritional interventions are used in critically ill patients. Nutrition is considered a palliative treatment. Dietary counseling, provision of nutritional support, and alleviation of diet-related issues should be an essential component of a holistic approach to palliative and end-of-life care. **Objective:** This study aimed to highlight the main clinical outcomes and guidelines on nutritional therapies and palliative care in critically ill cancer patients. **Methods:** The PRISMA Platform systematic review rules were followed. The search was carried out from June to August 2024 in the Scopus, PubMed, Science Direct, Scielo, and Google Scholar databases. The quality of the studies was based on the GRADE instrument and the risk of bias was analyzed according to the Cochrane instrument. **Results and Conclusion:** 133 articles were found. A total of 44 articles were evaluated in full and 22 were included and developed in the present systematic review study. Considering the Cochrane tool for risk of bias, the overall assessment resulted in 22 studies with a high risk of bias and 27 studies that did not meet GRADE and AMSTAR-2. Most studies showed homogeneity in their results, with X^2=75.7%>50%. It was concluded that according to the ESPEN and ASPEN guidelines, no differences in clinical outcomes were identified between numerous nutritional interventions, including increased energy or protein intake, parenteral nutrition or isocaloric enteral nutrition, supplemental parenteral nutrition or different mixed oil lipid injectable emulsions. However, clinical judgment and close monitoring along with appropriate palliative care are required. Decisionmaking in this field must be carried out on an individual basis, weighing the benefits and harms that may cause to patients' quality of life. The guidelines recommend that, if oral food intake remains inadequate despite counseling and oral nutritional supplements, enteral nutrition or, if this is not sufficient or feasible, parenteral nutrition (supplemental or total) should be considered.

Keywords: Critical patients. Cancer. Nutritional therapy. Palliative care.

Introduction

In the context of nutritional therapies, most critically ill patients are unable to provide their nutrition. These patients are often provided with artificial nutrition. Guidelines aim to summarize the evidence on nutritional support to guide professionals in providing artificial nutrition to critically ill patients and provide/update recommendations on several key issues that are central to providing nutritional support to most critically ill adult patients **[1]**.

In this regard, appropriate or precise nutritional interventions are used in critically ill patients. Nutrition is considered palliative care. Total parenteral nutrition may be recommended for patients who would otherwise die prematurely from starvation and malnutrition **[2]**.

Some randomized clinical trials on the use of oral, enteral, and supplemental parenteral nutrition in patients undergoing cancer therapy show some benefit in therapy adherence and some domains of quality of life. Some malnourished (hypophagic) patients with incurable cancer may survive longer thanks to parenteral nutrition, while limited data suggest that quality of life can be maintained for a limited period **[2,3]**.

Nutritional support for cancer patients in palliative care is essential to increase patient survival and quality of life. In the past, there has been limited collaboration between oncologists, clinical nutrition specialists, and palliative care physicians involved in the treatment of patients with advanced cancer **[3]**. For many years, efforts have been made to find a screening tool to identify patients in need of palliative care in a hospital setting **[4]**, as this would be very useful both in internal medicine and, in particular, in medical oncology **[5]**.

Palliative care was established in the United Kingdom 50 years ago **[6]**. In this country, general medical advice defines people approaching the end of life as those who are likely to die within the next 12 months **[7]**. More than a third of hospitalized cancer patients die or are transferred to hospice **[8]**. Research has reported that unplanned hospitalization for a patient with advanced cancer strongly predicts a median survival of less than 6 months **[9]**. However, identifying the needs of a palliative patient is far more important than the exact prognosis **[7]**.

It is necessary to define the most important variables in identifying the indication for nutritional support in cancer patients undergoing palliative care. A 2013 editorial indicated that palliative care is not an alternative to the end of curative treatments, but rather that it should be simultaneous and early **[10]**.

Dietary counseling, the provision of nutritional support, and the alleviation of diet-related issues should be an essential component of a holistic approach to palliative and end-of-life care. With the aging population and the increasing number of people living with not just one life-limiting illness, but several, the dietary management of these patients becomes more complex **[11]**.

Therefore, this study highlighted the main clinical results and guidelines on nutritional therapies and palliative care in critically ill cancer patients.

Methods

Study Design

This study followed the international systematic review model, following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) guidelines. Available at: http://www.prisma-statement.org/?AspxAutoDetectCookieSupport=1. Accessed on: July 18, 2024. The AMSTAR-2 (Assessing the Methodological Quality of Systematic Reviews) methodological quality standards were also followed. Available at: https://amstar.ca/. Accessed on: July 18, 2024.

Data Sources and Search Strategy

The literature search process was conducted from June to August 2024 and developed based on Scopus, PubMed, Lilacs, Ebsco, Scielo, and Google Scholar, covering scientific articles from various periods to the present day. The descriptors (DeCS / MeSH Terms) used were "Critical patients. Cancer. Nutritional therapy. Palliative care", and the Boolean expression "and" was used between MeSH terms and "or" between historical discoveries.

Study Quality and Risk of Bias

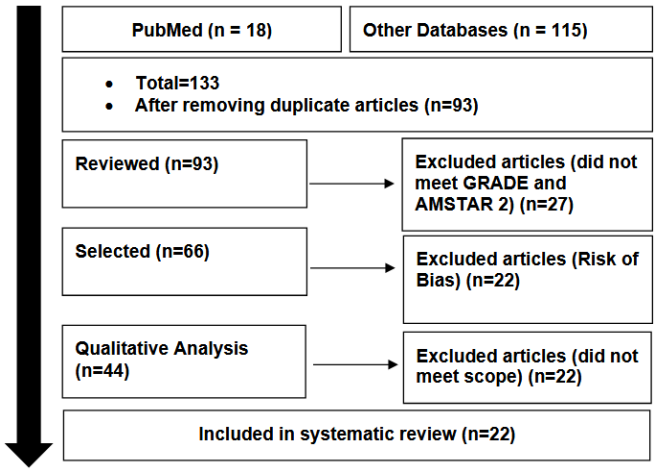
Quality was classified as high, moderate, low, or very low regarding risk of bias, clarity of comparisons, precision, and consistency of analyses. The most prominent findings were systematic reviews or meta-analyses of randomized controlled trials, followed by randomized clinical trials. Low-quality evidence was attributed to case reports, editorials, and brief communications, according to the GRADE instrument. Risk of bias was analyzed according to the Cochrane instrument by analyzing the funnel plot (sample size versus effect size) using Cohen's d test.

Results and Discussion

Summary of Findings

A total of 133 articles were found and submitted to eligibility analysis, with 22 final studies selected to comprise the results of this systematic review. The selected studies were of medium to high quality (Figure 1), considering the level of scientific evidence from studies such as meta-analysis, consensus, randomized clinical trials, prospective, and observational studies. Biases did not compromise the scientific basis of the studies. According to the GRADE instrument, most studies presented homogeneity in their results, with X^2= 75.7% > 50%. Using the Cochrane risk of bias tool, the overall assessment resulted in 22 studies with a high risk of bias and 27 studies that did not meet the GRADE and AMSTAR-2 criteria.

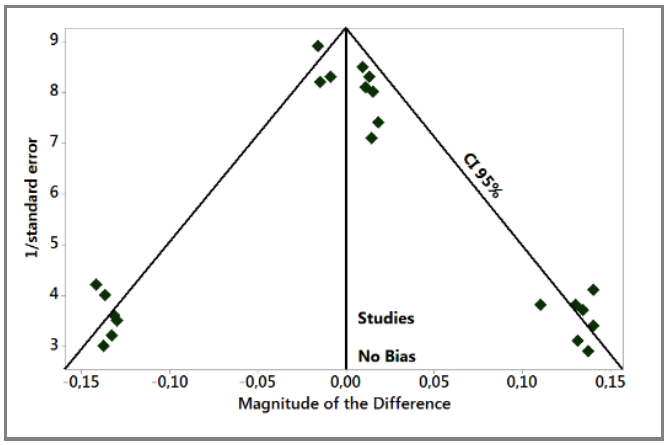
Figure 1. Flowchart showing the article selection process.



Source: Own authorship.

Figure 2 presents the results of the risk of bias of the studies using the funnel plot, showing the calculation of the effect size (magnitude of the difference) using Cohen's d test. Precision (sample size) was determined indirectly by the inverse of the standard error (1/Standard Error). This graph exhibited symmetrical behavior, suggesting no significant risk of bias, either among studies with small sample sizes (lower precision), shown at the bottom of the graph, or among studies with large sample sizes, shown at the top.

Figure 2. The symmetrical funnel plot suggests no risk of bias among the small sample size studies shown at the bottom of the graph. High-confidence and highly recommended studies are shown above the graph (n=22 studies).



Source: Own authorship.

Major Findings

According to the results of the literature search process, the authors of Oliveira et al. (2023) **[12]** identified, through a prospective cohort study, the clinical utility of assessing nutritional status using validated tools for indicating enteral nutrition for patients with incurable cancer in palliative care. Patients were assessed for nutritional risk using the Patient-Generated Subjective Global Assessment and for cancer cachexia (CC) using the modified Glasgow Prognostic Score at enrollment and after approximately 30 days. A total of 180 patients participated. The only nutritional status parameter associated with function was CC. The less severe the CC, the greater the likelihood that the Karnofsky Performance Status would remain stable or improve over 30 days (noncachectic: OR = 1.95; 95% CI, 1.01-3.47; malnourished: OR = 1.06; 95% CI, 1.01-1.42). Furthermore, white skin color (OR = 1.79; 95% CI, 1.04-2.47), higher education level (OR = 1.39; 95% CI, 1.13-2.78), and inadequate caloric intake (OR = 1.96; 95% CI, 1.02-2.81) were also associated with the outcome. Therefore, the use of the modified Glasgow Prognostic Score to identify the presence and severity of CHD, which is associated with function, has the potential to aid clinical decision-making regarding the indication of enteral nutrition in patients with incurable cancer receiving palliative care.

In this context, the role of nutritional support for cancer patients receiving palliative care remains controversial, in part because there is no consensus on the definition of a patient receiving palliative care due to the ambiguity in the common medical usage of the adjective "palliative." However, the guidelines recommend assessing nutritional deficiencies in all these patients because, regardless of whether they are still undergoing cancer treatment, malnutrition leads to poor performance status, impaired quality of life, unplanned hospitalizations, and reduced survival. Given

that nutritional interventions tailored to individual needs can be beneficial, the guidelines recommend that if oral food intake remains inadequate despite counseling and oral nutritional supplements, enteral nutrition or, if this is not sufficient or feasible, parenteral nutrition (supplemental or total) should be considered in suitable patients **[13]**.

The nutritional management of palliative care patients can raise ethical concerns, particularly when enteral nutrition is prescribed via nasogastric tube (NGT). SánchezSánchez et al. (2021) **[14]** conducted a systematic review to analyze the current state of enteral nutrition management via NGT in palliative care patients and its impact on their well-being and quality of life. The use of NGT tubes caused fewer episodes of diarrhea and more restrictions than the group that did not use NGT tubes. Furthermore, the use of tubes increased emergency room visits, although there was no contrast between NGT devices and percutaneous endoscopic gastrostomy (PEG). No statistical difference was found between the use of tubes (NGT and PEG) and non-use regarding symptom management, comfort level, and satisfaction at the end of life. However, it improved hospital survival compared to other procedures, and differences were found in hospitalizations related to the use of other tubes or devices.

Also, artificial nutrition can be integrated into a palliative care program when a positive influence on quality of life is expected and the risk of dying from malnutrition is greater than that due to cancer progression. The ESPEN guidelines suggest that enteral nutrition should be considered first whenever the gastrointestinal tract is functional and oral nutrition remains inadequate despite nutritional interventions **[15]**.

In this regard, enteral nutrition is most commonly used in palliative care patients with head and neck or upper gastrointestinal tract cancer. In these patients, the main indication for initiating enteral nutrition is oropharyngeal/esophageal dysphagia or gastric obstruction/dysmotility, due to mechanical and functional factors related to the disease, but also to palliative side effects induced by chemotherapy and/or radiotherapy **[16]**.

In patients with a life expectancy of several weeks or months who are unable to meet more than 60% of their daily energy requirements through oral intake in the long term, obtaining early gastrointestinal access is a useful strategy. Among gastric devices, the PEG is the gold standard, while a radiologically inserted gastrostomy or, occasionally, a surgical gastrostomy should be performed when an endoscopically guided tube cannot be placed. Long-term jejunal access (endoscopic or surgical jejunostomy) may be an option in the case of gastric obstruction/dysmotility. Placement of an NGT or nasojejunal tube may be considered when enteral nutrition is expected for the short term (usually up to 6 weeks) and/or survival is uncertain **[17]**.

In patients with head and neck cancer who are unable to swallow, the use of an enteral route via an NGT or gastrostomy may be an appropriate strategy for obtaining nutritional support in the home care setting **[16]**. According to a study evaluating the impact of home artificial nutrition (HAN) on performance status and survival in palliative cancer patients, enteral nutrition, with dysphagia as the main indication, can maintain/improve NGT and prolong median survival by up to 22.1 weeks (considering that death by starvation usually occurs within 2 months in healthy individuals, or even earlier in patients with advanced cancer without nutritional support) **[18,19]**.

In patients with esophageal cancer, PEG provides better nutritional status than self-expandable metal stents and is an independent factor associated with overall survival **[20]**. In these patients, endoscopically assisted NGT is also a viable palliative option, with a low complication rate, and for nutritional support, as it allows us to increase energy intake, serum albumin, median survival, and reduce hospitalization compared to zero oral nutrition **[21]**. However, Yu et al. **[22]** indicate a slightly worse quality of life in esophageal cancer patients receiving NGT feeding compared with percutaneous chemoradiotherapy. In a comprehensive assessment, it is reasonable to consider PEG as the preferred choice for long-term nutritional support in palliative esophageal cancer patients.

When enteral nutrition is contraindicated or unfeasible due to stricture, subobstruction/obstruction, dysmotility, peritoneal carcinomatosis, malabsorption, abdominal pain or intolerance, and severe discomfort, parenteral nutrition should be considered. Therefore, to choose the optimal nutritional access, a multidisciplinary clinical evaluation is strongly recommended, taking into account not only the primary and secondary tumor location (gastrointestinal vs. extragastrointestinal) and its direct/indirect effects on the digestive tract, but also the patient's overall situation, clinical condition, including cancer prognosis, nutritional status, performance status, quality of life, potential effects of nutritional support, and the wishes and expectations of the patient and their family **[15]**.

Conclusion

It was concluded that, according to the ESPEN and ASPEN guidelines, no differences in clinical outcomes were identified between numerous

nutritional interventions, including increased energy or protein intake, parenteral nutrition or isocaloric enteral nutrition, supplemental parenteral nutrition, or different mixed-oil lipid injectable emulsions. However, clinical judgment and close monitoring are necessary, along with appropriate palliative care. Decision-making in this area should be individualized, weighing the benefits and potential harms to patients' quality of life. The guidelines recommend that if oral food intake remains inadequate despite counseling and oral nutritional supplements, enteral nutrition or, if this is not sufficient or feasible, parenteral nutrition (supplemental or total) should be considered.

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The authors declare no conflict of interest.

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