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REVIEW ARTICLE

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Clinical outcomes and guidelines for nutrological therapy and palliative medicine in cancer patients: a systematic review

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Abstract

Introduction: Nutritional support for cancer patients in palliative care is still a controversial topic. Dietary counseling, providing nutritional support, and alleviating diet-related issues should be an essential components of a holistic approach to palliative and end-of-life care. **Objective:** It was to carry out a systematic review to explore and discuss the main approaches to nutritional therapy in palliative care in cancer patients. **Methods:** The PRISMA Platform systematic review rules were followed. The search was carried out from August to September 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:** 141 articles were found. A total of 46 articles were evaluated in full and 21 were included and developed in the present systematic review study. Considering the Cochrane tool for risk of bias, the overall assessment resulted in 23 studies with a high risk of bias and 28 studies that did not meet GRADE and AMSTAR-2. Most studies showed homogeneity in their results, with X^2=84.5%>50%. It was concluded that the use of the modified Glasgow Prognostic Score to identify the existence and severity of CC, which is associated with function, has the potential to assist in clinical decision-making regarding the indication of enteral nutrition in patients with incurable cancer undergoing palliative care. There are not enough quality studies that provide evidence of the improvement in health status and quality of life when using enteral nutrition through NGT in patients receiving palliative care. For this reason, decision-making in this field must be carried out on an individual basis, weighing up the benefits and harms that can be caused 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: Nutritional therapy. Palliative care. Chronic diseases. Survival.

Introduction

Although nutritional interventions are becoming widely used in cancer patients, the goals and outcomes of these treatments are not always well defined. This is because nutrition is traditionally considered a palliative treatment confined to the area of palliative care, whereas the modern approach includes nutrition as early supplementary support to improve patient adherence to oncological therapies, and total parenteral nutrition may be recommended in patients who would be destined to succumb sooner from starvation and malnutrition than from tumor progression **[1]**.

In this context, some randomized clinical trials on the use of oral, enteral, and supplemental parenteral nutrition in patients undergoing cancer therapy show some benefit in adherence to therapy and some domains of quality of life. Some malnourished (hyperphagic) patients with incurable cancer may survive longer thanks to parenteral nutrition, while few data suggest that quality of life can be maintained for a limited period **[1,2]**.

Nutritional support for cancer patients in palliative care remains a controversial topic. In the past, there has been limited collaboration between oncologists, clinical nutrition specialists, and palliative care physicians involved in the management of patients with advanced cancer **[2]**. For many years, efforts have been made to find a screening tool to identify patients in need of palliative care in a hospital setting **[3]**, as this would be very useful both in internal medicine and, in particular, in medical oncology **[4]**.

Palliative care was established in the United Kingdom 50 years ago **[5]**. 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 **[6]**. More than a third of hospitalized cancer patients die or are transferred to hospice **[7]**. Research has reported that an unplanned hospitalization for a patient with advanced cancer strongly predicts a median survival of less than 6 months **[8]**. However, it is much more important to identify the need than the exact prognosis of the palliative patient **[6]**.

Therefore, 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 **[9]**. 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. With the aging of the population and the increase in the number of people living with not just one limiting disease, but with several, the dietary treatment of these patients becomes more complex **[10]**.

Given the above, this study carried out a systematic review to explore and discuss the main approaches to nutritional therapy in palliative care for 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) rules. Available at: http://www.prisma-statement.org/?AspxAutoDetectCookieSupport=1. Accessed on: 08/21/2024. The AMSTAR-2 (Assessing the methodological quality of systematic reviews) methodological quality standards were also followed. Available at: https://amstar.ca/. Accessed on: 08/21/2024.

Data Sources and Search Strategy

The literature search process was carried out from August to September 2024 and developed based on Scopus, PubMed, Lilacs, Ebsco, Scielo, and Google Scholar, covering scientific articles from various periods to the present day. The following descriptors (DeCS /MeSH Terms) were used: "Nutritional therapy. Palliative care. Chronic diseases. Survival", and the Boolean "and" was used between the MeSH terms and "or" between the historical findings.

Study Quality and Risk of Bias

Quality was classified as high, moderate, low, or very low regarding the risk of bias, clarity of comparisons, precision, and consistency of analyses. The most evident emphasis was on systematic review articles or meta-analyses of randomized clinical trials, followed by randomized clinical trials. Low quality of evidence was attributed to case reports, editorials, and brief communications, according to the GRADE instrument. The risk of bias was analyzed according to the Cochrane instrument by analyzing the Funnel Plot graph (Sample size versus Effect size), using Cohen's d test.

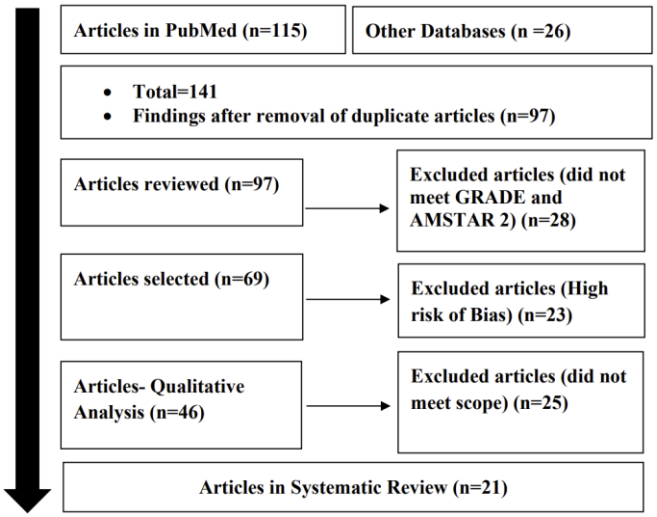
Results and Discussion

Summary of Findings

A total of 141 articles were found that were submitted to eligibility analysis, and 21 final studies were selected to compose the results of this systematic review. The studies listed were of medium to high quality (Figure 1), considering the level of scientific evidence of studies such as meta-analysis, consensus, randomized clinical, prospective, and observational. 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=84.5%>50%. Considering the Cochrane tool for risk of bias, the overall assessment resulted in 23 studies with a high risk of bias and 28 studies that did not meet GRADE and AMSTAR-2.

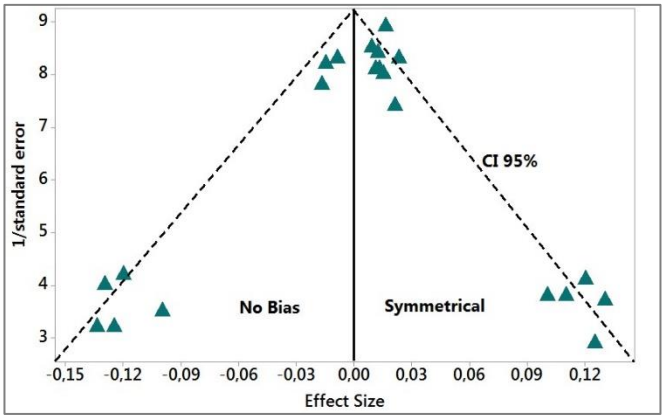
Figure 1. Flowchart showing the article selection process.



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 Test (d). Precision (sample size) was determined indirectly by the inverse of the standard error (1/Standard Error). This graph had a symmetrical behavior, not suggesting a significant risk of bias, both among studies with small sample sizes (lower precision) that are shown at the bottom of the graph and in studies with large sample sizes that are shown at the top.

Figure 2. The symmetrical funnel plot does not suggest a risk of bias among the studies with small sample sizes that are shown at the bottom of the graph. Studies with high confidence and high recommendation are shown above the graph (n=21 studies).



Source: Own authorship.

Major Clinical Findings

The authors of Oliveira et al. (2023) **[11]** 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 (non-cachectic: 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 existence and severity of CC, which is associated with function, has the potential to aid in clinical decision-making regarding the indication of enteral nutrition in patients with incurable cancer in palliative care.

In this context, the role of nutritional support for cancer patients in palliative care remains a controversial topic, partly because there is no consensus on the definition of a patient in palliative care due to the ambiguity in the common medical use of the adjective palliative. However, the guidelines recommend assessing nutritional deficiencies in all these patients because, regardless of whether they are still undergoing anticancer 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 **[12]**.

The nutritional management of patients in palliative care can raise ethical issues, especially when enteral nutrition is prescribed via nasogastric tube (NGT). The authors Sánchez-Sánchez et al. (2021) **[13]** analyzed through a systematic review the current state of management of enteral nutrition via NGT in patients in palliative care and its effect on their well-being and quality of life. The use of NGT caused fewer episodes of diarrhea and more restrictions than the group that did not use NGT. In addition, the use of tubes increased emergency department 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) or not, concerning symptom management, level of comfort, and satisfaction at the end of life. However, it improved hospital survival compared to other procedures, and differences were found in hospitalizations to the use of other tubes or devices.

Artificial nutrition can be integrated into a palliative care program when a positive influence on the quality of life is expected and the risk of dying from malnutrition is greater than due to cancer progression **[14]**. 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 **[14]**.

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 **[15]**.

In patients with a life expectancy of several weeks or months who are unable to meet more than 60% of their long-term daily energy requirements through oral intake, early gastrointestinal access is a useful strategy. Among gastric devices, PEG is the gold standard, while radiologically inserted gastrostomy or eventually 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 short-term enteral nutrition is expected (usually up to 6 weeks) and/or survival is uncertain **[16]**.

In addition, in patients with head and neck cancer who are unable to swallow, the use of enteral feeding via NGT or gastrostomy may be an appropriate strategy for obtaining nutritional support in the home care setting **[15]**. According to a study evaluating the impact of home artificial nutrition on performance status and survival in palliative oncology patients, enteral nutrition, with dysphagia as the main indication, can maintain/improve KPS 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) **[17,18]**.

In patients with esophageal cancer, PEG allows better nutritional status than selfexpandable metal stents and is an independent factor associated with overall survival **[19]**. 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 via oral route **[20]**. However, Yu et al. **[21]** indicate a slightly worse quality of life in patients with esophageal cancer receiving NGT feeding compared with percutaneous feeding during chemoradiotherapy. In a comprehensive assessment, it is reasonable to consider PEG as the preferred choice for long-term nutritional support in palliative patients with esophageal cancer. When enteral nutrition is contraindicated or unfeasible due to stenosis, sub-obstruction/obstruction, dysmotility, peritoneal carcinomatosis, malabsorption, abdominal pain or intolerance, and severe discomfort, parenteral nutrition should be considered **[14]**.

Therefore, to choose the optimal nutritional access, a multidisciplinary clinical assessment is strongly recommended, taking into account not only the primary and secondary location of the tumor (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 members **[14]**.

Conclusion

It was concluded that the use of the modified Glasgow Prognostic Score to identify the existence and severity of cancer cachexia, which is associated with function, has the potential to aid in clinical decision-making regarding the indication of enteral nutrition in patients with incurable cancer in palliative care. There are not enough high-quality studies that provide evidence of the improvement of health status and quality of life of the use of enteral nutrition through nasogastric tube in patients in palliative care. For this reason, decision-making in this field should be carried out on an individualized basis, weighing the benefits and harms that it may cause to the quality of life of patients. 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.

CRediT

Author contributions **Conceptualization**- Ricardo de Oliveira Carvalho, Lucila Maria de Almeida Lopes, Karlla

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Informed Consent

It was applicable.

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No additional data are available.

Conflict of Interest

The authors declare no conflict of interest.

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It was applied by Ithenticate®.

Application of Artificial Intelligence (AI)

Not applicable.

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It was performed.

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