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REVIEW ARTICLE

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Major outcomes of clinical studies and guidelines on nutrological therapy and palliative care in critically ill patients: a systematic review

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Abstract

Introduction: Adequate nutritional therapy is often a missing factor in the treatment of patients receiving end-of-life palliative care. The American Academy of Hospice and Palliative Care defined palliative care as comprehensive and specialized care. The main concerns are nutritional, pain, and symptom management, information sharing and advance care planning, psychosocial and spiritual support, and care coordination. **Objective:** It was to list the main outcomes of clinical studies and guidelines on enteral/parenteral nutritional therapy and palliative care in critically ill patients. **Methods:** The systematic review rules of the PRISMA Platform 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:** A total of 93 articles were found. A total of 44 articles were evaluated in full and 16 were included and developed in the present systematic review study. Considering the Cochrane tool for risk of bias, the overall assessment resulted in 13 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=85.9%>50%. It was concluded that palliative nutritional care plans for critically ill patients should be managed by a nutritionist together with patients and family members. The benefits and risks of artificial nutrition and hydration should be discussed with the patient and/or caregiver when palliative care is initiated. The main goal of palliative care is to preserve the patient's quality of life. This includes defending freedom of choice and allowing the patient to determine their level of nutritional intervention. The results suggest that providing nutritional support (~12 g of protein, 300 kcal) daily prevents the loss of active tissue mass in palliative cancer patients. Based on these results, we recommend the inclusion of this simple nutritional support to prevent malnutrition in cancer patients in palliative care. Furthermore, severe malnutrition is a predictor of reduced survival in patients with advanced gastrointestinal cancer. Information on nutritional status should be considered to individualize the palliative care

plan for these patients and, therefore, improve their quality of life. Using the modified Glasgow Prognostic Score to identify the existence and severity of cancer cachexia has the potential to aid clinical decision-making regarding the indication of enteral nutrition in patients with incurable cancer receiving palliative care.

Keywords: Critical patients. Nutrological therapy. Palliative care.

Introduction

Adequate nutritional therapy is often a missing factor in the treatment of patients receiving end-of-life palliative care. Clinicians focus primarily on pain management and providing comfort for these patients. However, the American Academy of Hospice and Palliative Care defines palliative care more broadly: "Palliative care is comprehensive, specialized care provided by an interdisciplinary team to patients and families living with a serious or life-threatening advanced illness that is expected to progress toward death and where care is particularly focused on alleviating suffering and promoting quality of life. Primary concerns include pain and symptom management, information sharing and advance care planning, psychosocial and spiritual support, and care coordination." **[1]**.

In addition, maintaining or improving nutritional or hydration status, when feasible as part of basic or routine interventions, should be addressed for end-of-life care **[2]**. In the setting of nutritional therapies, most critically ill patients are unable to provide their nutrition. In these patients, artificial nutrition is often provided. The guidelines aim to summarize the evidence on nutritional support to guide professionals in providing artificial nutrition to critically ill patients and to provide/update recommendations on several key issues that are central to providing nutritional support to most critically ill adult patients **[3]**.

In this regard, appropriate or precise nutritional interventions are used in critically ill patients. Nutrition is considered a palliative treatment. Total parenteral nutrition may be recommended in patients who would otherwise die from starvation and malnutrition **[4]**. 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 (hypophagia) 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 **[4-7]**.

Therefore, it is necessary to define the most important variables in identifying the indication for nutritional support in cancer patients undergoing palliative care **[8,9]**. 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, 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 **[11]**.

Therefore, the present study listed the main outcomes of clinical studies and guidelines on enteral/parenteral nutritional therapy and palliative care in critically ill 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: 08/20/2024. The AMSTAR-2 (Assessing the methodological quality of systematic reviews) methodological quality standards were also followed. Available at: https://amstar.ca/. Accessed on: 08/20/2024.

Data Sources and Search Strategy

The literature search process was carried out 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 following descriptors (DeCS/MeSH Terms) were used: "Critical patients. Cancer. Nutritional therapy. Palliative care", 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-analysis 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

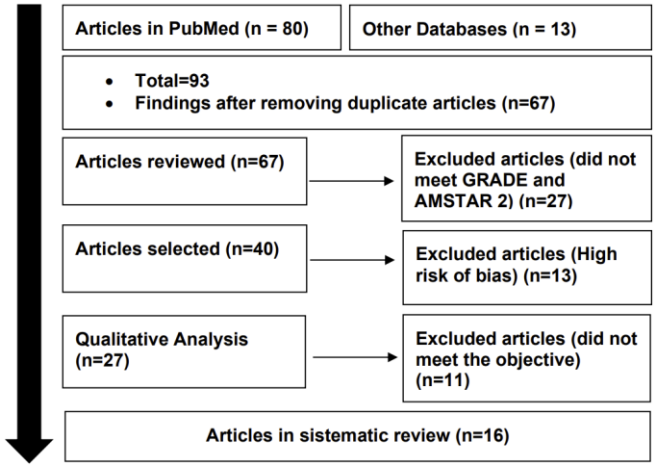
the Cochrane instrument by analyzing the Funnel Plot graph (Sample size versus Effect size), using Cohen's d test.

Results and Discussion

Summary of Findings

A total of 93 articles were found and submitted to eligibility analysis, with 16 final studies 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=85.9%>50%. Considering the Cochrane tool for risk of bias, the overall assessment resulted in 13 studies with a high risk of bias and 27 studies that did not meet GRADE and AMSTAR-2.

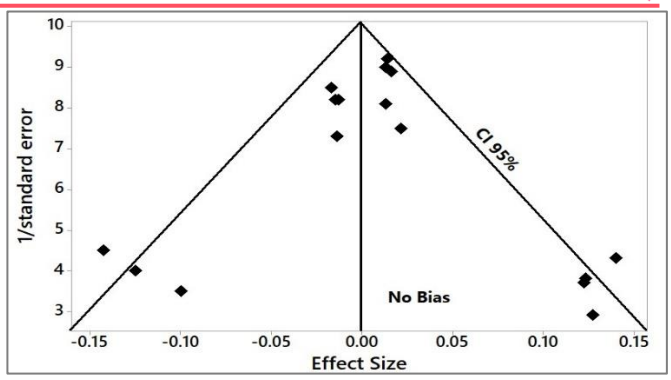
Figure 1. Flowchart showing the article selection process.



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. High confidence and high recommendation studies are shown above the graph (n=16 studies).



Source: Own authorship.

Major Findings

As part of the palliative care process, dietary restrictions in a critically ill patient should be removed. According to McCann **[12]**, patients with advanced dementia should be kept comfortable in the least restrictive environment, with every effort made to remove dietary restrictions. As the patient's dietary intake declines, the clinician should assess the continued need for therapeutic medications, such as insulin. Nutritional support by tube feeding or total parenteral nutrition (TPN) is warranted as a treatment for patients receiving palliative care. Studies indicate that patients with advanced dementia who have lost weight and have difficulty eating do not fare better with the initiation of tube feeding. Evidence does not support the use of enteral feeding to prolong life, improve function, prevent aspiration pneumonia, or reduce pressure ulcers **[13]**. Other articles recommend revisiting the clinical issue of feeding patients with dementia and older patients and challenging the assumption that tube feeding is beneficial **[14,15]**. For the terminally ill patient, artificial nutrition may not be the solution **[16]**. Randomized trials of TPN have also indicated only minimal value or benefit to the patient, and in some cases, survival rates have been shortened with this nutritional support **[17,18]**.

The issue of dehydration and its effect on critically ill patients has been the subject of many studies. The terminally ill patient does not experience the acute symptoms of headache, vomiting, and abdominal cramps that accompany dehydration in a healthy person. A prospective study of 31 terminally ill cancer patients and 1 stroke patient examined how giving patients food and fluids on demand affected their quality of life. Dietary restrictions were lifted, and patients were asked throughout the day whether they were hungry, thirsty, or had dry mouth. Two-thirds of the patients never felt hungry; the others felt hungry but lost their appetite over time. Thirst and dry mouth were common in 21 patients and persisted until death in 12 of these patients. Comfort care, such as moistening the lips and offering ice chips or fluids on request, has been shown

to reduce the sensation of thirst **[19]**.

In critically ill patients, metabolic changes of hemoconcentration and hyperosmolality with subsequent azotemia, hypernatremia, and hypercalcemia are thought to produce a sedative effect on the brain. Reduced oral secretions, coughing, and frequent urination are desirable effects of reduced hydration. The medical literature provides further support for the concept that neither nutrition nor hydration provides comfort or improves the quality of life in patients receiving palliative care **[20]**.

Furthermore, intensive care units (ICUs) have significant palliative care needs but lack a reliable care structure. A study by Salins et al. (2024) **[21]** brought together 40 systematic reviews, and 6 main themes were generated that reflect palliative and end-oflife care practices in ICUs and their outcomes. Effective communication and accurate prognoses have enabled families to make informed decisions, cope with uncertainty, alleviate suffering, and shorten ICU stays. Exceptional end-of-life care should include symptom management, family support, optimization of hydration and nutrition, avoidance of futile treatments, and grief support.

The implementation of nutritional support is a basic need for patients in oncology palliative care. Given this, the authors Ticha et al. (2023) **[22]** designed a controlled clinical study with 63 patients (mean age 61.3 years, mean range 32–82 years). Patients were assigned to group A (no nutritional support n = 39 patients) or group B (sips as nutritional support n = 24 patients). Patients were assessed by noninvasive methods: body weight, waist and upper arm circumference, triceps skinfold thickness, bioimpedance analysis, and dynamometry. Quality of life was assessed using modified questionnaires. In contrast to group A, group B did not experience significant weight loss, i.e., A: 81.9 ± 15.8–80.5 ± 15.8 kg (P = 0.028) and B: 73.9 ± 14.9–73 ± 16 kg. In contrast to group B, patients in group A showed small variations in their health status, thus decreasing their scores to the significance limit. The results suggest that providing nutritional support (~12 g protein, 300 kcal) daily prevents active tissue mass loss in palliative oncology patients.

Mao et al. (2024) **[23]** analyzed the nutritional status and its prognostic effect on the survival of patients with advanced gastrointestinal cancer through a prospective cohort study. The study consisted of 202 patients with advanced gastrointestinal (GI) cancer from a palliative care unit. The following data were collected from the patients: biochemical indicators, i.e., anemia (hemoglobin levels), albumin, prealbumin, C-reactive protein (CRP), and anthropometric parameters, i.e., body mass index (BMI), nutritional status by Patient-Generated Subjective Global Assessment (PG-SGA), and performance status by Karnofsky Performance Status (KPS). Severe malnutrition was confirmed with a PG-SGA score ≥ 9. Severe malnutrition was found in 71.3% of patients according to the PG-SGA cutoff. PG-SGA score ≥ 9, albumin level < 35 g/L, and CRP level ≥ 10 mg/L predicted shorter life expectancy. The results of multivariate Cox regression analysis showed that PG-SGA score ≥ 9 and albumin level < 35 g/L were predictive of reduced survival in these patients.

The authors of Oliveira et al. (2023) **[24]** demonstrated 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 ~30 d. A total of 180 patients participated. The only nutritional status parameter that was associated with function was WC. The less severe the CHD, the more likely 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). In addition, white skin color (OR = 1.79; 95% CI, 1.04-2.47), higher educational level (OR = 1.39; 95% CI, 1.13-2.78), and inadequate calorie intake (OR = 1.96; 95% CI, 1.02-2.81) were also associated with outcome. Therefore, using the modified Glasgow Prognostic Score to identify the presence and severity of cancer cachexia has the potential to aid clinical decision-making regarding the indication for enteral nutrition in patients with incurable cancer receiving palliative care.

The nutritional management of patients in palliative care can raise ethical issues, especially when enteral nutrition is prescribed by a nasogastric tube (NGT). The authors Sánchez-Sánchez et al. (2021) **[25]** analyzed through a systematic review the current state of enteral nutrition management by NGT in patients under 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 room attendance, although there was no contrast between NGT and percutaneous endoscopic gastrostomy (PEG) devices. No statistical difference was found between the use of tubes (NGT and PEG) or not, about 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. Furthermore, 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 higher 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 **[26]**.

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 **[27]**.

Conclusion

It was concluded that palliative nutritional care plans for critically ill patients should be managed by a nutritionist together with patients and family members. The benefits and risks of artificial nutrition and hydration should be discussed with the patient and/or caregiver when palliative care is initiated. The main goal of palliative care is to preserve the patient's quality of life. This includes defending freedom of choice and allowing the patient to determine their level of nutritional intervention. The results suggest that providing nutritional support (~12 g protein, 300 kcal) daily prevents active tissue mass loss in palliative cancer patients. Based on these results, we recommend the inclusion of this simple nutritional support to prevent malnutrition in cancer patients receiving palliative care. Furthermore, severe malnutrition is a predictor of reduced survival in patients with advanced gastrointestinal cancer. Information on nutritional status should be considered to individualize the palliative care plan for these patients and, therefore, improve their quality of life. Using the modified Glasgow Prognostic Score to identify the presence and severity of cancer cachexia has the potential to aid clinical decision-making regarding the indication for enteral nutrition in patients with incurable cancer receiving palliative care.

CRediT

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The authors declare no conflict of interest.

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