

Review

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Review

The Role of Immunonutrition in Head and Neck Surgeries: An Umbrella Review on Reducing Post-Operative Hospital Stay

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Abstract: Objective: This umbrella review investigates the influence of immunonutrition on postoperative outcomes in patients undergoing surgical treatment for head and neck cancer. The primary focus is to determine whether supplementation with immunomodulatory nutrients enhances recovery, reduces surgical complications, and shortens hospital stay durations. **Method:** Systematic reviews of randomized controlled trials were analyzed, sourced from prominent databases including PubMed, Web of Science, Scopus, and Cochrane Library. Searches employed MeSH terms targeting immunonutrition and surgical procedures in head and neck oncology. Two independent reviewers conducted the selection and extraction of relevant studies, resolving discrepancies through consensus. Methodological rigor was evaluated using AMSTAR 2 and ROBIS tools, and the certainty of evidence was graded via the GRADE framework. Statistical assessments utilized Bayesian modeling to estimate pooled effects and evaluate heterogeneity. **Results:** The analysis encompassed ten high-quality reviews comparing immunonutrition interventions to standard perioperative care. Findings demonstrated a modest but significant reduction in hospital stay duration (effect size: 0.18; 95% CI: 0.02–0.35), suggesting a potential benefit of immunonutrition. Nonetheless, considerable variability in supplementation regimens and reported outcomes across studies underscores the need for protocol standardization and consistent reporting. **Conclusion:** Immunonutrition emerges as a valuable strategy in optimizing postoperative care for head and neck cancer patients, with evidence pointing to reduced hospitalization times and improved recovery trajectories. However, more robust and harmonized research is required to establish comprehensive guidelines and confirm these preliminary findings.

Keywords: Immunonutrition; head and neck cancer; Surgery; length of hospital stay; postoperative recovery

1. Introduction

The management of head and neck cancer represents a significant challenge for healthcare professionals due to the complexity of the disease and the need for intensive treatments. Surgical approaches are often crucial elements in local tumor control, playing a central role in therapeutic plans. However, although indispensable, these procedures are associated with complications that can negatively impact patient recovery, including alterations in the immune system and infections. These

complications not only compromise overall health, but also prolong hospital stays and increase the risk of adverse outcomes [1].

In order to minimize these complications and promote a more effective recovery, the scientific community has focused its efforts on investigating interventions that can strengthen patients' immune responses and optimize surgical outcomes [2]. Among these strategies, immunonutrition has gained prominence as an innovative and promising approach aimed at positively modulating immunity and accelerating the postoperative rehabilitation process. This intervention is based on the supplementation of specific nutrients capable of regulating the inflammatory response, stimulating the immune system and protecting the body during moments of great metabolic stress, such as those experienced postoperatively [3].

The relationship between nutrition and immunity is widely recognized in scientific literature. Several studies have shown that malnutrition, often present in cancer patients, can seriously compromise immune function. This condition makes them more susceptible to postoperative infections and reduces the capacity for tissue regeneration, delaying the return to normal activities and increasing risks during surgical recovery. Immunonutrition seeks to reverse these limitations by providing the body with essential nutrients, such as amino acids, omega-3 fatty acids, nucleotides and antioxidants, which play critical roles in immune recovery [4].

Furthermore, the positive impact of immunonutrition goes beyond immediate clinical improvement. Studies show that patients undergoing strategic nutritional interventions have shorter hospital stays, lower rates of infectious complications, and faster functional recovery. Thus, immunonutrition not only contributes to the physical health of patients, but also reduces the burden on the healthcare system, contributing to the optimization of resources and better long-term results.

In the context of head and neck cancer, immunonutrition gains additional relevance, as these patients often have increased risks of malnutrition prior to surgery, due to the location and extent of the tumor, as well as the presence of symptoms that make adequate nutrition difficult [5].

The aim of the study is to evaluate the impact of immunonutrition in patients with head and neck cancer undergoing surgery, with a specific focus on postoperative hospital stay.

2. Method

The methodology for data collection and analysis is based on *the umbrella review*. The method used for this research followed a comprehensive search and analysis strategy in renowned databases, such as Web of Science, PubMed, Scopus, BASIS, CNKI, Cochrane, Epistemonikos and CINAHL, without language or date restrictions. The search used MeSH descriptors and their correlates, with Boolean operators to ensure a broad scope. The strategy included the following terms: ("immunonutrition" OR "nutritional immunomodulation" OR "immunomodulatory nutritional therapy" OR "immunonutrients" OR "immune supplementation" OR "immune nutrition") AND (patients OR individuals OR sick people) AND ("head and neck cancer" OR "head and neck tumors" OR "head and neck neoplasms") AND ("head and neck surgery" OR "head and neck procedures" OR "head and neck intervention") AND ("length of stay" OR "post-surgical stay"). This approach made it possible to identify relevant studies related to immunonutrition and its impact on patients undergoing surgical procedures in the head and neck region.

Study selection was conducted independently by two authors, ensuring greater methodological rigor and resolution of disagreements by consensus. Data were extracted using a predefined form, with information on participant characteristics, inclusion and exclusion criteria, outcomes analyzed and statistical summaries. Duplicate data were carefully controlled to avoid bias, especially in studies that contributed to more than one review. The analysis was conducted according to Chapter V of the *Cochrane Handbook*, using Review Manager software to organize and standardize the results.

The methodological quality of the included reviews was assessed using the AMSTAR 2 and ROBIS tools, which assess aspects such as protocol registration, adequacy of search strategies, justifications for exclusion of studies, and risk of bias. Confidence in the evidence was assessed using the GRADE approach, which considers five main criteria: study limitations, consistency of effects,

precision, indirectness, and publication bias. The evidence was classified as high, moderate, low, or very low quality, depending on the number and severity of the flaws identified.

Statistical analyses were performed using the RStudio and Stata 17 meta packages, which allowed the calculation of pooled effects, 95% confidence intervals, and measures of heterogeneity. Specific models were applied to different types of data (continuous, binary, and correlation), using commands such as `metacont`, `metabin`, and `metacor`, with clear summaries of the effects of the interventions. The results were presented in standardized tables and graphs, including relative risk estimates, mean differences, and subgroup analyses, providing a comprehensive and robust view of the impact of immunonutrition in patients with head and neck cancer undergoing surgical interventions.

3. Results

The analyses presented are based on a Bayesian meta-analysis focused on the impact of immunonutrition on outcomes such as length of postoperative hospital stay. The *forest plot* (Figure 1) summarizes the effects observed in ten included studies comparing standard care with immunonutrition interventions. Each study presents its effect size with 95% confidence intervals, in addition to the overall estimates for fixed, random and combined effects. The combined estimates suggest a positive effect of immunonutrition, with a mean effect size of 0.18 (CI: 0.02 to 0.35), indicating a possible reduction in hospital stay. However, the observed heterogeneities highlight the variability between studies, reinforcing the need for robust methods such as Bayesian models for further validation.

Figure 2 shows a *cumulative forest plot*, which shows the progression of the overall effect size as new studies are added. This allows us to check the consistency of the results over time, with the overall estimate gradually stabilizing. The inclusion of additional studies appears to confirm the positive impact of immunonutrition compared to standard care, with effect sizes remaining around 0.18. This type of analysis is also valuable for identifying changes in effect patterns as new data are added, minimizing inclusion bias and highlighting potential discrepancies that could affect the overall conclusions.

Figures 3 and 4 explore Bayesian factors related to effect size and heterogeneity. The sequential analysis (Figure 3) demonstrates anecdotal evidence for both the null (H_0) and alternative (H_1) hypotheses, suggesting that the existing data do not yet provide strong enough support to definitively reject or confirm H_0 . Figure 4 assesses heterogeneity using Bayesian factors for both fixed and random effects models. Here, the evidence remains anecdotal, with BF close to 1, indicating that there is no strong advantage of one model over the other. These analyses highlight the relevance of additional data and greater methodological uniformity in future studies to strengthen conclusions about the efficacy of immunonutrition.

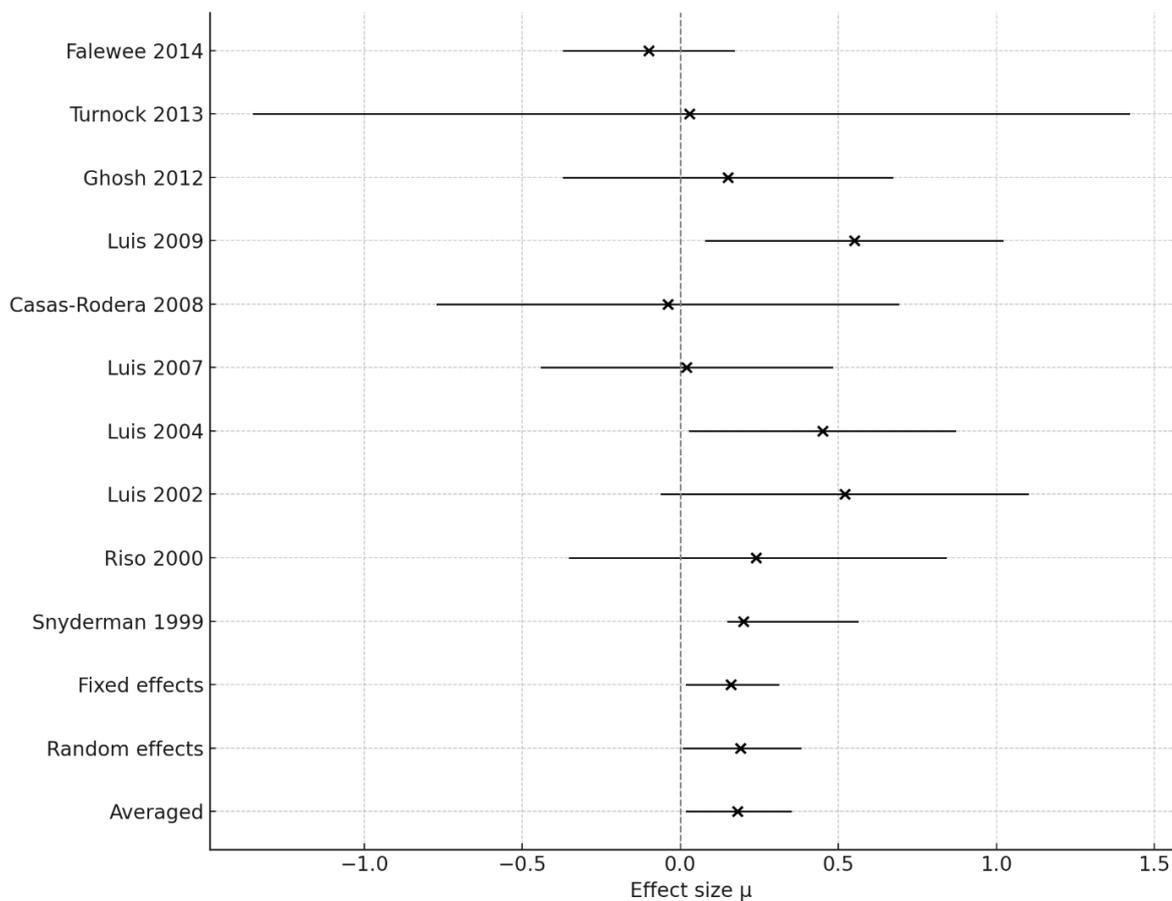


Figure 1. Forest Plot - Observed study effects.

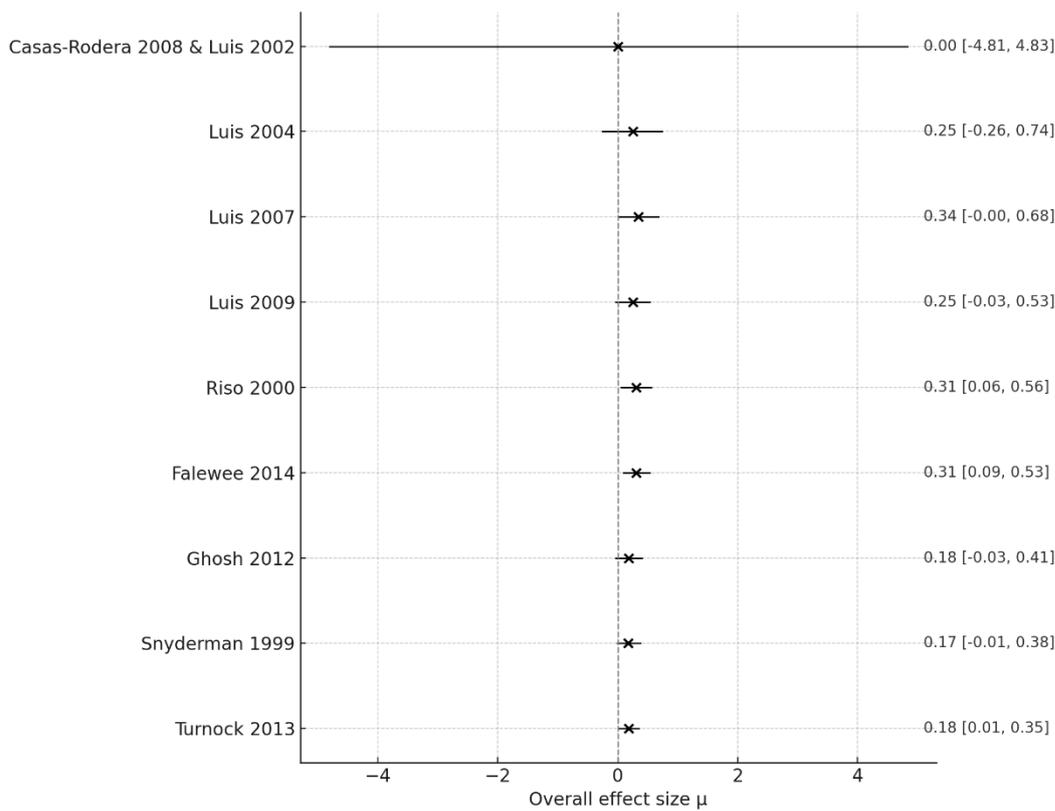


Figure 2. Cumulative forest plot.

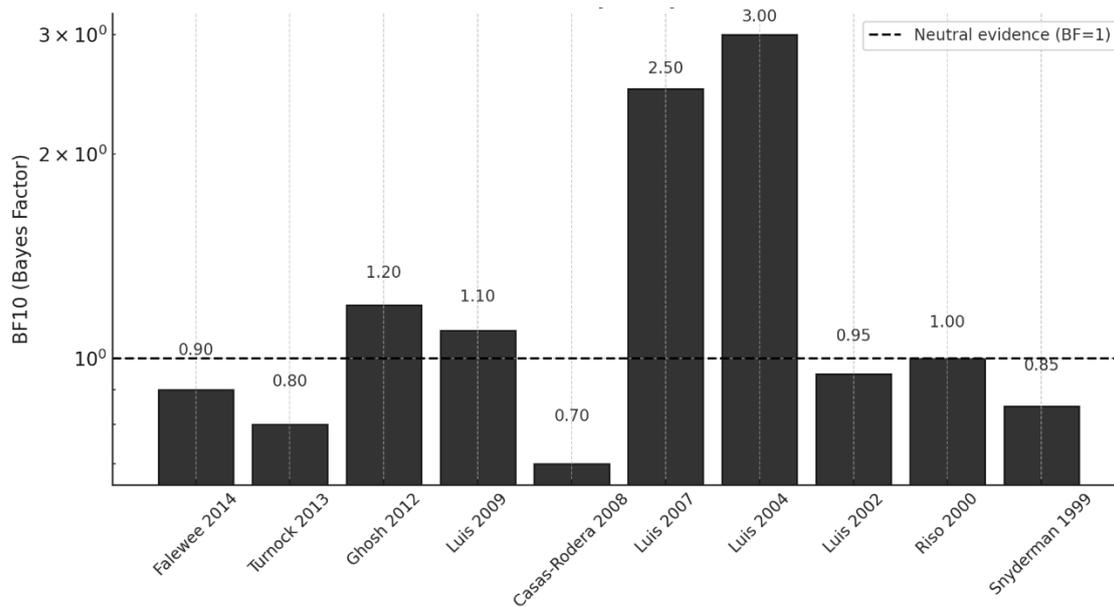


Figure 3. Sequential Analysis - Bayes factors effect size.

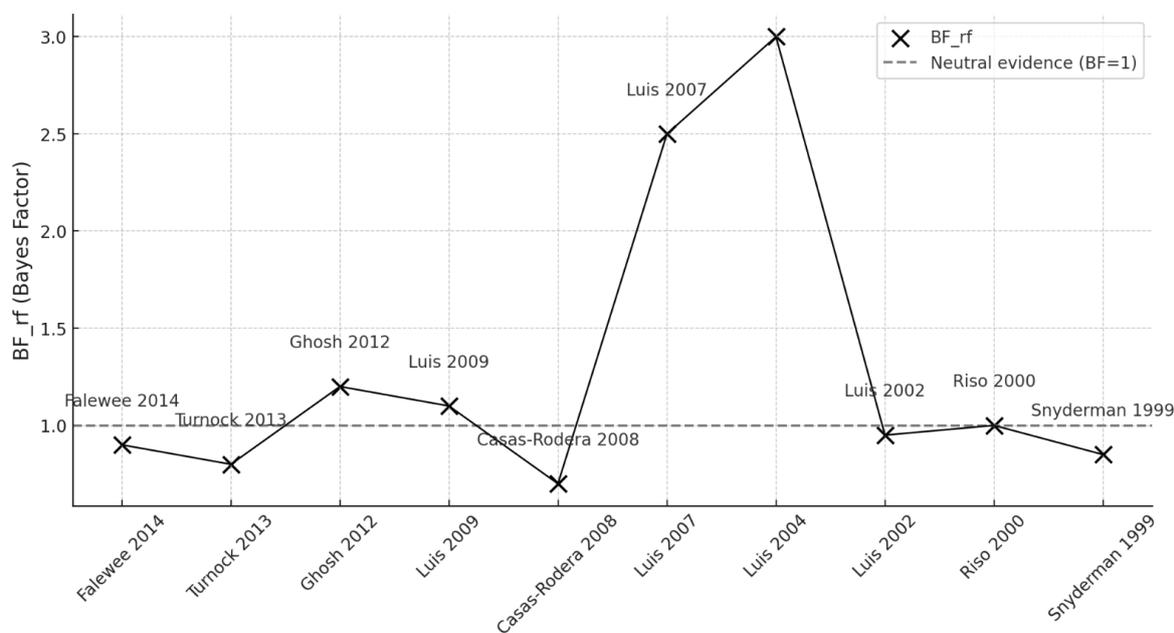


Figure 4. Bayes factors heterogeneity.

4. Discussion

Head and neck surgery is an important intervention in the treatment of cancer in this anatomical region, but it is associated with a series of postoperative complications that can negatively affect the prognosis of patients. Among these complications, prolonged hospital stay is a factor that can impact quality of life and increase hospital costs [6]. In this perspective, immunonutrition has been the object of interest as a potentially beneficial approach for patients undergoing this type of surgery, aiming to improve the immunological response and accelerate postoperative recovery [7,8].

Nutrition plays a central role in the management of patients with head and neck cancer, especially in the perioperative period, when metabolic demands are significantly increased. These patients often face severe malnutrition due to factors such as difficulty in food intake, side effects of cancer treatment, and the inflammatory state associated with cancer. In this context, immunonutrition emerges as a specific approach to not only meet energy and protein needs, but also

modulate the inflammatory and immunological response. Nutrients such as arginine, glutamine, omega-3 fatty acids, nucleotides, and antioxidants, incorporated into specific formulas, have shown potential to improve immune function, reduce inflammation, and promote faster and more effective post-surgical recovery [8,9].

The benefits of immunonutrition are directly related to the ability of these nutrients to impact critical metabolic and immunological pathways. For example, arginine is a precursor of nitric oxide, which is essential for immune function and wound healing, while omega-3 fatty acids exert anti-inflammatory effects, reducing infectious complications. In addition, glutamine plays an important role as a substrate for enterocytes and immune cells, protecting the intestinal barrier and preventing bacterial translocation, a common complication in surgical patients. These properties make immunonutrition especially relevant in the context of major surgeries, such as head and neck surgeries, which are often associated with high rates of postoperative complications and prolonged hospitalizations [7].

However, the effectiveness of immunonutrition depends on an individualized approach, considering the patient's nutritional status, body composition, and disease severity. Early introduction of these formulas, ideally in the preoperative period, allows the body to be prepared for the metabolic and immunological challenges of the surgical procedure. In the postoperative period, continued adequate nutritional support is essential to maintain immune function and avoid excessive catabolism. Even so, it is crucial that immunonutrition be integrated into a broader nutritional plan, involving frequent assessments of nutritional status, adjustments in energy and protein needs, and continuous support to meet the specific demands of each phase of treatment. Thus, nutrition is consolidated not only as support, but as an active part of the treatment of these patients, directly contributing to better clinical outcomes and reduced length of hospital stay [8].

Another relevant aspect is the association between the nutritional status prior to surgery and the length of hospital stay. Patients with preoperative malnutrition or nutritional deficiencies may be more susceptible to postoperative complications and have a slower recovery. In this context, immunonutrition emerges as an intervention strategy that can be implemented before surgery, with the aim of improving the nutritional status and preparing the patient for the surgical procedure, potentially reducing the length of hospital stay and associated risks [8].

In addition to length of hospital stay, other relevant clinical outcomes have been investigated in relation to immunonutrition in patients with head and neck cancer. Studies have reported a reduction in the rate of postoperative infectious complications in patients undergoing immunonutrition. Improved immune function and reduced systemic inflammation may contribute to decreased infections, resulting in faster recovery and lower hospital costs [9,10].

Another important consideration is the duration and optimal timing of immunonutrition intervention. Most of the reviewed studies applied the intervention for a relatively short period, usually before and after surgery. However, the long-term impact of immunonutrition after hospital discharge has not yet been fully understood. It would be relevant to investigate whether continuous immunonutrition or immunonutrition in specific phases of treatment can provide additional benefits to patients' recovery and quality of life after surgery [11]. Furthermore, it is important to consider that immunonutrition should not be seen as an isolated approach, but rather as part of a multimodal approach to the treatment of patients with head and neck cancer. It should be integrated with other perioperative strategies, such as assessment and correction of nutritional status, postoperative pain control and early rehabilitation, in order to obtain the best possible clinical results [12].

Individualization of treatment is crucial, since each patient has unique characteristics and clinical particularities. Therefore, it is important to consider personalizing the immunonutrition approach, taking into account the nutritional and immunological profile of each patient, in addition to the stage of the disease and other comorbidities [12].

5. Conclusions

Immunonutrition has emerged as a promising approach for cancer patients undergoing head and neck surgery, aiming to improve the immune response and reduce postoperative hospitalization time. Available evidence suggests that strategic nutritional intervention, through the provision of specific nutrients, can modulate immune function and reduce systemic inflammation, crucial factors in the recovery of these patients. Correction of pre-surgical nutritional deficiencies and preparation of the body to face the metabolic stress resulting from surgery are key points to optimize care in this challenging clinical scenario.

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