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Perioperative Nutritional Supplementation to Reduce Postoperative Infections: A Systematic Review and Meta-Analysis

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INTRODUCTION

Postoperative infections, including surgical site infections (SSIs), pneumonia, bloodstream infections (BSIs), and urinary tract infections (UTIs), remain among the most frequent and impactful complications following surgery. They contribute substantially to patient morbidity, length of stay, and healthcare costs, despite improvements in surgical techniques and perioperative care. In Europe alone, healthcare-associated infections are estimated to cause over 90,000 deaths annually and impose a burden of more than 500 DALYs per 100,000 population [1]. Despite the adoption of ERAS protocols and prophylactic antibiotics, the incidence of postoperative infections has plateaued in many settings, suggesting the need for adjunctive strategies beyond standard perioperative care. In this context, perioperative nutrition has emerged as a potentially modifiable factor capable of influencing immune responses, gut microbiota, and systemic inflammation. Immunonutrition (enriched with arginine, omega-3 fatty acids, nucleotides), probiotics, synbiotics, and protein supplementation are currently being investigated for their ability to prevent infectious complications and improve surgical outcomes [2,3]. However, the literature is fragmented and results are often inconsistent across interventions and populations [4-7].

OBJECTIVES

This study aimed to systematically evaluate the efficacy of perioperative nutritional supplementation in reducing postoperative infectious complications in adult surgical patients. The focus on infection stems from its clinical burden and its potential sensitivity to immune-modulating strategies. Secondary outcomes included specific infection types (SSIs, BSIs, UTIs, and pneumonia) and hospital length of stay (LOS), selected for their relevance to patient recovery and healthcare system impact. These outcomes were selected to capture both the direct impact of infections and their broader consequences on patient recovery and resource utilization.

METHODS

A systematic review and meta-analysis were conducted in accordance with PRISMA 2020 guidelines and registered in PROSPERO (CRD42024575184) [8]. PubMed, Scopus, Cochrane Library, and Google Scholar were searched without restrictions on date or language. Eligible studies included adult surgical patients receiving perioperative nutritional interventions (immunonutrition, probiotics, synbiotics, protein supplementation) compared to standard care or placebo. The research question was structured using the PICO framework to ensure structured and clinically meaningful comparisons. Both randomized controlled trials (RCTs) and observational studies were included. The primary outcome was the incidence of infectious complications. Meta-analyses were performed using STATA SE 19, with pooled odds ratios (ORs) and 95% confidence intervals (CIs). Heterogeneity was assessed via the I^2 statistic, and a random- or fixed-effects model was applied accordingly. The methodological quality of included

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studies was assessed using NIH tools, with most RCTs classified as low or moderate risk of bias, and observational studies showing greater variability [9]. Risk of bias was independently assessed by multiple reviewers, and disagreements were resolved by consensus, ensuring rigorous evaluation.

RESULTS

Thirty-nine studies (27 RCTs and 12 observational) met the inclusion criteria. Immunonutrition was the most consistently effective intervention, significantly reducing the overall incidence of infectious complications in both RCTs (OR = 0.36; 95% CI: 0.21–0.62) and observational studies (OR = 0.32; 95% CI: 0.17–0.61). The protective effect was particularly evident with oral administration and in patients aged ≤65 years. Probiotics showed a borderline protective effect overall, while synbiotics appeared more effective in younger patients and when administered orally. Protein supplementation was evaluated in too few studies to allow for pooled analysis of the primary outcome.

Regarding secondary outcomes, a general trend of benefit was observed across most interventions, though with variability in effect size and consistency. Immunonutrition and protein supplementation were associated with reduced SSIs. Probiotics showed favorable effects on UTIs and pneumonia. Synbiotics were linked to a shorter LOS, though heterogeneity and limited data warrant cautious interpretation. The quality of evidence varied, with most RCTs showing low or moderate risk of bias. These findings, although promising, should be interpreted with caution due to limited data in some subgroups and moderate heterogeneity in certain analyses.

CONCLUSIONS

Perioperative nutritional supplementation, particularly immunonutrition, represents a promising and evidence-based strategy to reduce postoperative infectious complications. Secondary benefits on SSIs, UTIs, pneumonia, and LOS support the broader integration of nutritional protocols into surgical care. Immunonutrition showed the most consistent results, while probiotics were effective for UTIs and pneumonia. Synbiotics significantly reduced LOS, though limited data and heterogeneity warrant caution. The strength of evidence depends on study volume and quality; thus, interventions like immunonutrition for SSIs should be prioritized, while others—such as protein supplementation for non-SSI outcomes—require further evaluation. Clarifying differential impacts across surgical specialties and standardizing formulations, timing, and administration routes will be crucial for tailored and effective implementation.

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