

The Impact of Preoperative Nutrition-Based Prehabilitation on the Severity of Postoperative Complications in Patients with Esophageal Cancer: A Systematic Review and Meta-Analysis

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Abstract:

Background and Objective: Evaluating the effects of nutritional prehabilitation on postoperative complications in patients with esophageal cancer can not only contribute to optimizing clinical outcomes but also represents a key step toward evidence-based care and reducing variability in current treatment practices. This systematic review and meta-analysis aimed to critically analyze the existing evidence regarding the impact of preoperative nutrition-based prehabilitation on the severity of postoperative complications in patients with esophageal cancer.

Materials & Methods: This systematic review and meta-analysis, conducted in accordance with PRISMA guidelines, aimed to assess the effects of preoperative nutrition-based prehabilitation—with or without adjunctive physical and psychological interventions—on the severity of postoperative complications in patients with esophageal cancer. A comprehensive literature search was conducted in five international and two Iranian databases up to September 2025. Only randomized controlled trials (RCTs) were included. Nutritional prehabilitation was defined as the administration of oral supplements or enteral nutrition for a minimum of 7 days, and some studies also incorporated physical training and psychological support. Data extraction, quality assessment, and statistical analyses were performed independently by two reviewers. Risk ratios (RR), weighted mean differences (WMD), and I^2 statistics for heterogeneity were used for data synthesis. Analyses were conducted using RevMan software, and a p-value of <0.05 was considered statistically significant.

Results: Five RCTs involving a total of 405 patients were included in this systematic review and meta-analysis. The pooled analysis demonstrated a significant reduction in the incidence of severe postoperative complications in favor of preoperative nutritional prehabilitation (RR = 0.66, 95% CI: 0.48–0.92). Similarly, a comparable reduction was observed in studies employing multimodal prehabilitation (RR = 0.69, 95% CI: 0.49–0.97).

Conclusion: The findings of this systematic review and meta-analysis suggest that preoperative nutrition-based prehabilitation—particularly when implemented as part of a multimodal program—can effectively reduce the severity of postoperative complications in patients undergoing surgery for esophageal cancer. Nutritional interventions should be considered an essential component of preoperative care in this patient population.

Keywords: Esophagectomy, Complication Severity, Postoperative, Nutritional Prehabilitation

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Background and Objective

Esophageal cancer is one of the most challenging malignancies of the upper gastrointestinal tract, with an increasing global incidence and a generally poor prognosis.¹ In advanced stages, it typically requires aggressive treatments, including surgery, which is associated with a high risk of postoperative complications.² Despite notable advances in surgical techniques and postoperative care, postoperative complications remain a major determinant of survival, quality of life, and healthcare costs.³

Among the many factors influencing postoperative outcomes, patients' nutritional status holds particular significance. Malnutrition is commonly observed in patients with esophageal cancer due to dysphagia, reduced appetite, and systemic effects of the disease, and is associated with immunosuppression, delayed wound healing, increased risk of infections, and other surgical complications.⁴ Epidemiological studies have shown that more than half of patients with esophageal cancer present with some degree of malnutrition before surgery.⁵

In this context, the concept of "prehabilitation" has been introduced, aimed at improving the physiological, functional, and nutritional status of patients prior to major surgery.⁶ One of the core components of prehabilitation is targeted nutritional intervention, which may include high-calorie diets, protein supplements, omega-3 fatty acids, and specialized nutritional support.⁷ These strategies may enhance patients' physiological resilience to surgical stress and help reduce postoperative complication rates.⁸

Preliminary evidence indicates that nutritional interventions as part of prehabilitation may positively influence surgical outcomes in patients with upper gastrointestinal cancers, particularly esophageal cancer.⁹ Some studies have reported reduced rates of postoperative infections, shorter hospital stays, and even decreased mortality following nutritional prehabilitation.¹⁰ However, other research

has yielded inconsistent findings, with some studies failing to show significant benefits.¹¹

Given the conflicting evidence and lack of consensus in the current literature, a comprehensive systematic review and meta-analysis specifically focused on patients with esophageal cancer is warranted.¹²⁻¹⁴ A systematic review allows for the aggregation, evaluation, and synthesis of primary study findings to offer a broader and more evidence-based perspective, thereby enhancing clinical decision-making.¹⁵⁻¹⁷ A meta-analysis further enables statistical estimation of the true effect size of interventions and strengthens the conclusions.¹⁸⁻²⁵

Moreover, subgroup analysis of different patient populations, types of nutritional interventions, and their effects on specific outcomes—such as the severity and type of complications (e.g., infection, anastomotic leakage, respiratory failure) and length of hospital stay—constitutes another key objective of such a review.²⁶⁻³⁰

A more detailed understanding of the physiological mechanisms through which preoperative nutrition can enhance postoperative recovery may also inform the design of more effective future interventions.³¹

In addition, policymakers can use the findings of this review to guide the standardization of prehabilitation protocols in hospitals and clinical settings.¹⁷ This can play a critical role in reducing the economic burden of surgical complications, improving treatment outcomes, and enhancing healthcare quality.¹⁸

Investigating the effects of nutritional prehabilitation on postoperative complications in patients with esophageal cancer not only supports optimization of treatment outcomes but also contributes significantly to the development of evidence-based care and reduction of variation in clinical practice. This systematic review and meta-analysis aims to synthesize current evidence on the effectiveness of preoperative nutrition-based prehabilitation

in mitigating the severity of postoperative complications in this patient population.

Materials and Methods

This systematic review and meta-analysis adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The primary objective was to assess the effect of preoperative nutritional prehabilitation (with or without exercise and/or psychological support) on the severity of postoperative complications in patients with esophageal cancer undergoing surgery. The secondary aim was to determine whether prehabilitation could reduce hospital length of stay (LOS), readmission rates, and mortality compared to standard care.

A comprehensive search was conducted in five international electronic databases—PubMed, Web of Science, Embase, Cochrane Library, and CINAHL—as well as two Iranian databases—SID and IranDoc—covering all English-language publications up to the end of August 2025. No restrictions were placed on country of origin or study design. Reference lists of included studies and related systematic reviews were also screened manually to identify any additional eligible trials. The search strategy was structured according to the PICOS framework, with a focus on: P (Population): Patients with esophageal and/or gastric cancer; I (Intervention): Preoperative prehabilitation including nutritional support with or without exercise and/or psychological support.

After removing duplicates, two reviewers independently screened titles and abstracts for eligibility. Any disagreements were resolved by a third reviewer. Eligible studies were included if they: Were randomized controlled trials (RCTs); Involved adult patients (≥ 18 years) diagnosed with esophageal cancer and scheduled for surgery; Provided separate analysis for esophageal cancer if other cancer types were also included.

The nutritional intervention was defined as the administration of oral nutritional supplements or enteral nutrition with or without dietary counseling for at least 7 days

prior to surgery, aiming to alter macronutrient intake (carbohydrates, proteins, and fats). Studies were included only if a nutritional intervention was a component of the prehabilitation. In unimodal prehabilitation, only nutritional support was delivered, whereas in multimodal prehabilitation, two or three components (nutrition, exercise, and/or psychological support) were implemented, with nutrition being a mandatory element. Control groups either received standard daily diets or nutrition counseling only. In some trials, high-risk patients (less than 50% of the control group) were allowed to receive similar interventions as the experimental group. Postoperative care protocols, such as enhanced recovery after surgery (ERAS), were comparable between groups.

Data were independently extracted by two reviewers using a pre-tested form, and discrepancies were resolved by a third reviewer. Extracted data included: (1) baseline patient characteristics, (2) details of the intervention, and (3) reported outcomes. If data were incomplete, corresponding authors were contacted. Data management and extraction were conducted using Zotero (version 6.0.26, Corporation for Digital Scholarship, USA) and Microsoft Excel (version 2305, Microsoft Corp., USA).

The risk of bias in included RCTs was assessed using the Cochrane Risk of Bias tool across six domains. Bias levels were classified as low, high, or unclear. Assessments were performed independently by two reviewers, and disagreements were resolved by a third. All assessments were completed using Review Manager software (RevMan version 5.4.1, Cochrane Collaboration, UK).

Forest plots were generated to assess the effect of prehabilitation on postoperative outcomes. For categorical data, pooled risk ratios (RRs) were calculated; for continuous data, either weighted mean differences (WMD) or standardized mean differences (SMD) with 95% confidence intervals (CIs) were used. Heterogeneity was assessed using the I^2 statistic. If I^2 was $< 50\%$ or $p > 0.1$, a fixed-effects model was applied; otherwise, a random-effects model was used. Where

studies reported medians and interquartile ranges (IQRs) instead of means and standard deviations (SDs), conversion formulas were used to estimate the mean and SD. All statistical analyses were performed using RevMan version 5.4.1. A p-value <0.05 was considered statistically significant.

Findings

The initial search yielded 501 articles. After screening titles, abstracts, and full texts and removing duplicates, a total of 5 studies were included in the final analysis. These 5 randomized controlled trials encompassed a total of 405 patients. The mean age of participants ranged from 60 to 70 years across studies.

Table 1. Summary of studies included in this systematic review

<i>First Author/ Year/ Country</i>	<i>Sample Size</i>	<i>Mean Age (years)</i>	<i>Neoadjuvant Therapy</i>	<i>Exercise/ Psychological Intervention</i>	<i>Type of Intervention</i>	<i>Main Outcome</i>	<i>Study Quality</i>
<i>L. J. Halliday/ 2021/UK</i>	187	57.66	No	No	<i>A tailored program based on symptoms, dietary habits, and nutritional deficiencies before surgery.</i>	<i>Nutritional intervention significantly reduced the severity of postoperative complications.</i>	<i>Good</i>
<i>T.Janssen/ 2021/ Netherlands</i>	95	64.57	Yes	Yes	<i>A preoperative program tailored to dietary habits and nutritional deficiencies.</i>	<i>Nutritional intervention significantly reduced the severity of postoperative complications.</i>	<i>Good</i>
<i>K.Liu/ 2020/China</i>	50	62.24	No	Yes	<i>A dietary plan was provided based on individual nutritional needs.</i>	<i>Nutritional intervention significantly reduced the severity of postoperative complications.</i>	<i>Good</i>
<i>L.C.Dewberry /2019/USA</i>	22	67.30	No	No	<i>A dietary plan was provided based on nutritional requirements.</i>	<i>Nutritional intervention significantly reduced the severity of postoperative complications.</i>	<i>Good</i>
<i>E.M.Minnella /2018/ Canada</i>	51	67.3	No	No	<i>A tailored preoperative plan based on symptoms, dietary habits, and nutritional deficiencies.</i>	<i>Nutritional intervention significantly reduced the severity of postoperative complications.</i>	<i>Moderate</i>

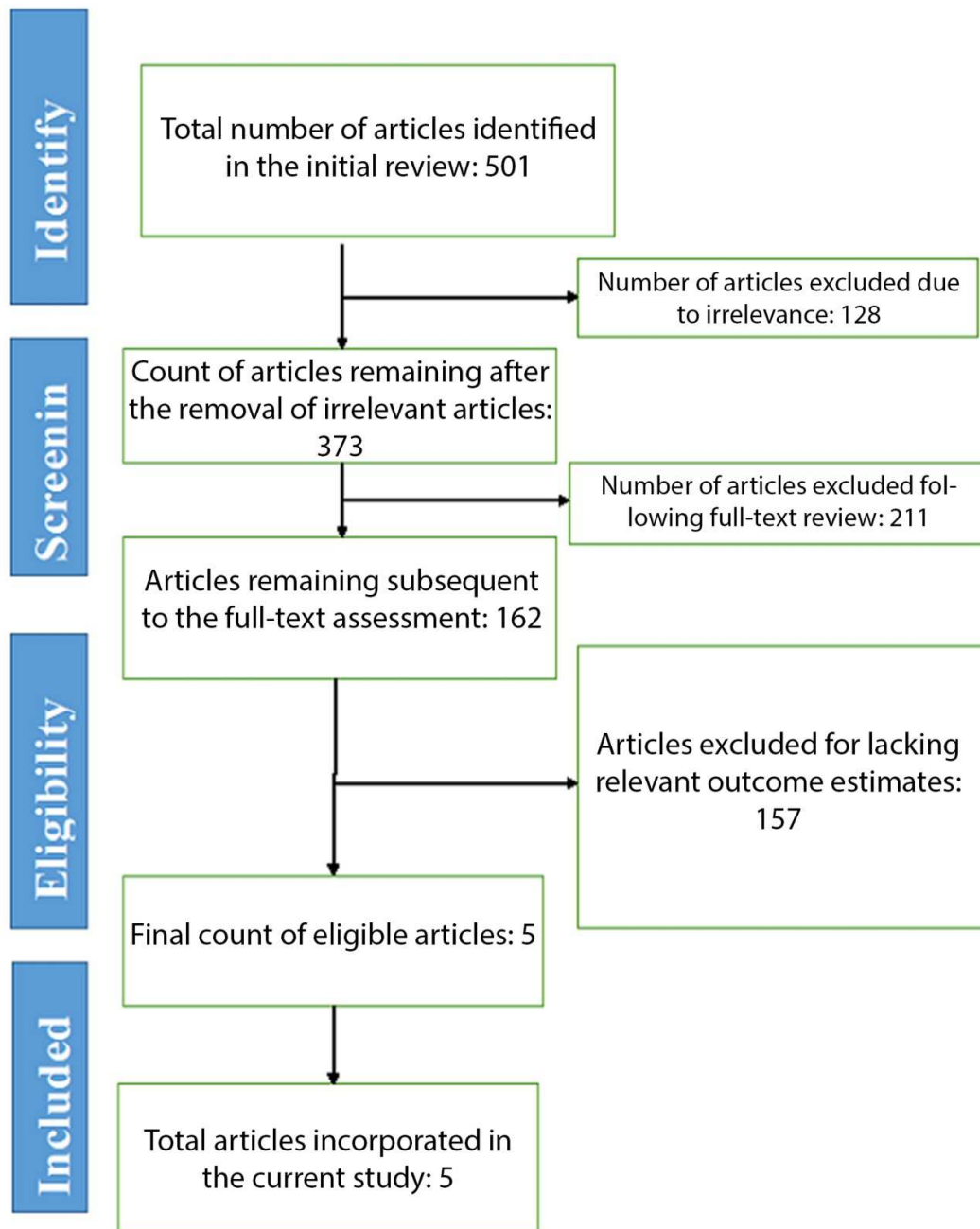


Diagram 1 - The process of inclusion and exclusion of studies in the present systematic review and meta-analysis

Severe postoperative complications

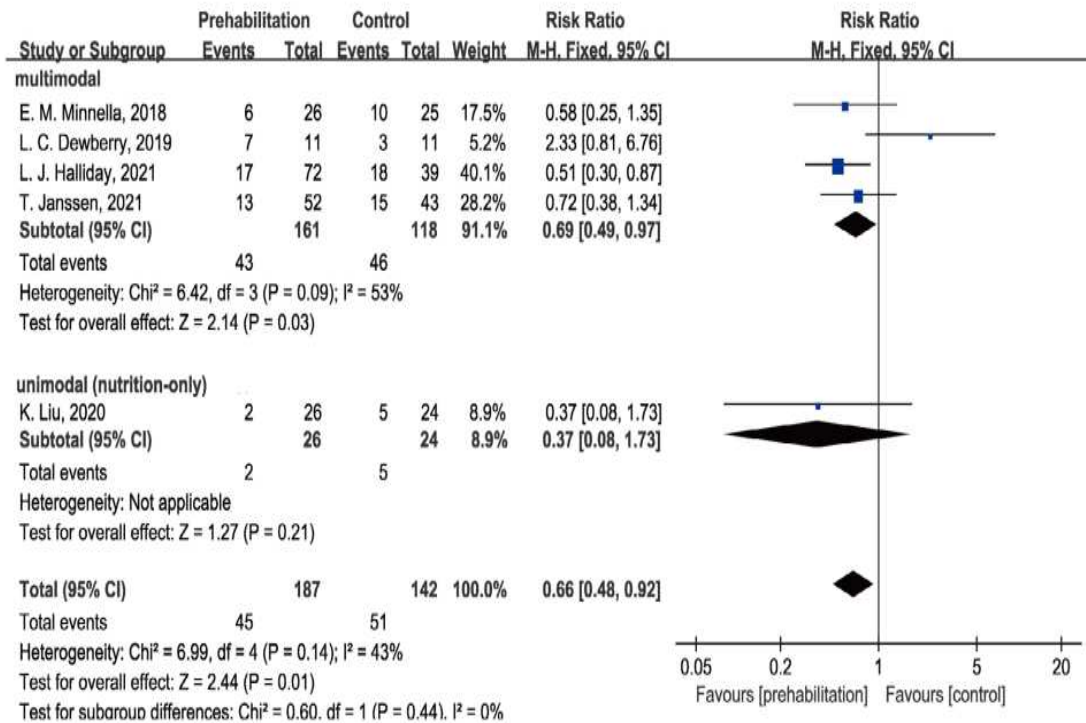


Figure 1. Forest plot evaluating the effect of preoperative nutrition-based prehabilitation on the incidence of severe postoperative complications

Among the included studies: Three incorporated exercise interventions as part of prehabilitation. Only one study included a psychological support component alongside nutritional support. One study involved patients who had received neoadjuvant therapy before surgery. All studies used nutrition-based prehabilitation interventions, and all reported a statistically significant reduction in the severity of postoperative complications in the intervention groups compared to controls (see Table 1). These findings support the effectiveness of both unimodal and multimodal prehabilitation strategies in improving postoperative outcomes among patients with esophageal cancer.

Severe postoperative complications—defined as grade III or higher according to the Clavien-Dindo classification—were reported in all five studies (Halliday et al., Janssen et

al., Liu et al., Dewberry et al., and Minnella et al.). As illustrated in Figure 1, preoperative nutrition-based prehabilitation significantly reduced the incidence of severe postoperative complications. The pooled risk ratio (RR) for any form of prehabilitation was 0.66 (95% CI: 0.48–0.92), indicating a 34% risk reduction compared to standard care. A similar effect was observed in multimodal prehabilitation interventions (which included nutrition combined with exercise and/or psychological support), with a pooled RR of 0.69 (95% CI: 0.49–0.97) (figure 1).

Discussion

The findings of this systematic review and meta-analysis demonstrate that preoperative nutrition-based prehabilitation can significantly reduce the severity of postoperative complications in patients undergoing surgery for esophageal cancer.

The risk of severe complications was 34% lower in the group receiving nutritional prehabilitation compared to controls, indicating the substantial effectiveness of this intervention.¹⁸

The results also suggest that studies incorporating multimodal prehabilitation—a combination of nutrition, exercise, and psychological interventions—reported a similarly significant reduction in severe complications. This indicates that integrating multiple supportive components may enhance overall efficacy, although nutrition remains the central element in such programs.¹⁹

Several mechanisms may explain the observed benefits of nutritional prehabilitation. Optimizing nutritional status before surgery enhances protein reserves and immune function, both of which are critical in managing surgical stress and promoting wound healing.²⁰ Additionally, oral nutritional supplements (ONS) or enteral feeding may correct deficiencies such as hypoalbuminemia and vitamin depletion, which are closely associated with complications like infection, anastomotic leakage, and delayed tissue repair.²¹

In patients with esophageal cancer, who frequently suffer from malnutrition due to dysphagia, anorexia, and neoadjuvant therapies, nutritional support becomes even more crucial. Improving nutritional status prior to surgery may serve as a protective factor against postoperative morbidity.²²

Studies that included exercise interventions as part of prehabilitation reported even greater benefits. Aerobic and resistance training prior to surgery can enhance patients' functional capacity and resilience to surgical stress.²³ Meanwhile, psychological interventions, such as counseling, education, or motivational interviewing, may reduce preoperative anxiety and improve adherence to dietary and physical activity recommendations, thereby reinforcing the overall impact of the program.²⁴

Although not all included studies were of high methodological quality, the consistency of results showing a reduction in severe

postoperative complications strengthens the reliability of the findings.²⁵ Furthermore, low statistical heterogeneity supports the validity of pooled effect estimates.²⁶

One of the strengths of this review is its focus on a specific population (patients with esophageal cancer) and inclusion of studies that explicitly implemented nutritional components. This approach enhanced sample homogeneity and ensured targeted evaluation of a key intervention that is often overlooked in previous reviews.²⁷ However, limitations include the limited number of eligible studies and variability in the type and duration of nutritional interventions.²⁸

Another point worth noting is that in some studies, patients in the control group received partial or similar interventions, particularly among high-risk patients. This may have reduced the observed differences between groups. Nevertheless, the statistically significant impact of nutritional prehabilitation confirms its clinical relevance.²⁹

It is also important to consider that while nutrition-based prehabilitation is effective, its final impact may depend on factors such as baseline nutritional status, disease stage, functional capacity, and type of surgery.³⁰ Thus, a one-size-fits-all approach may not be optimal, and individualized, tailored interventions are recommended to maximize outcomes.³¹

Conclusion

This systematic review and meta-analysis indicates that preoperative nutrition-based prehabilitation, particularly when delivered as part of a multimodal intervention, can play a crucial role in reducing severe postoperative complications in patients with esophageal cancer. Nutritional interventions should be considered a mandatory component of preoperative care in this patient population. Future research with larger sample sizes and rigorous study designs is recommended to provide stronger evidence and support the inclusion of nutritional prehabilitation in clinical guidelines.

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