Efficacy and Safety of Home Enteral Nutrition in Esophageal Cancer Patients: A Meta-Analysis Postprint

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Abstract

Background: Esophageal cancer patients frequently suffer from malnutrition. Domestic and international studies have shown that malnutrition significantly impacts patient recovery. Currently, an increasing number of patients continue to receive enteral nutrition support at home, but the effectiveness and safety of home enteral nutrition for esophageal cancer patients remain unclear.

Objective: To evaluate the effects of home enteral nutrition on nutritional status, complications, and quality of life in esophageal cancer patients through meta-analysis.

Methods: RCTs on the application effects of home enteral nutrition in esophageal cancer patients were searched in PubMed, the Cochrane Library, EMbase, Web of Science, CINHAL, ScoPus, Wanfang, CNKI, VIP, and Chinese Biomedical Literature Database from inception to November 1, 2022. The quality of included studies was assessed using the Cochrane risk-of-bias tool RoB 2.0, and meta-analysis was performed using RevMan 5.4.1 software.

Results: A total of 14 studies were included, involving 1040 esophageal cancer patients. Meta-analysis results showed that home enteral nutrition prevented weight loss [SMD=0.63, 95%CI (0.40, 0.85), P<0.00001] and BMI reduction [SMD=0.60, 95%CI (0.44, 0.76), P<0.00001], and improved serum nutritional indicators such as HLB [SMD=1.58, 95%CI (1.37, 1.79), P<0.00001]; additionally, it improved physical function [MD=6.67, 95%CI (2.86, 10.48), P=0.0006] and reduced fatigue symptoms [MD=-7.31, 95%CI (-11.85, -2.77), P=0.002], without increasing the incidence of complications [RR=1.33, 95%CI (1.00, 1.77), P=0.05].

Conclusion: Home enteral nutrition can improve the nutritional status and physical function of postoperative discharged esophageal cancer patients, and reduce

their fatigue symptoms, without increasing the incidence of gastrointestinal complications, but no improvement in overall quality of life was found.

Full Text

The Efficacy and Safety of Home Enteral Nutrition in Patients with Esophageal Cancer: A Meta-Analysis

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Abstract

Background: Malnutrition is highly prevalent among esophageal cancer patients and has been shown to significantly impede recovery. While an increasing number of patients continue to receive enteral nutrition support at home, the effectiveness and safety of home enteral nutrition (HEN) for this population remain unclear.

Objective: To evaluate the impact of HEN on nutritional status, complications, and quality of life in esophageal cancer patients through meta-analysis.

Methods: We systematically searched PubMed, the Cochrane Library, EMbase, Web of Science, CINHAL, Scopus, Wanfang, CNKI, VIP, and CBM for randomized controlled trials (RCTs) examining HEN in esophageal cancer patients from database inception to November 1, 2022. Study quality was assessed using the Cochrane Risk of Bias tool (RoB 2.0), and meta-analysis was performed using RevMan 5.4.1.

Results: Fourteen RCTs comprising 1,040 esophageal cancer patients were included. Meta-analysis revealed that HEN prevented weight loss [SMD=0.63, 95%CI (0.40, 0.85), $P<0.00001$] and BMI decline [SMD=0.60, 95%CI (0.44, 0.76), $P<0.00001$], and improved serum nutritional markers including hemoglobin [SMD=1.58, 95%CI (1.37, 1.79), $P<0.00001$]. Additionally, HEN improved physical function [MD=6.67, 95%CI (2.86, 10.48), P=0.0006] and reduced fatigue symptoms [MD=-7.31, 95%CI (-11.85, -2.77), P=0.002], without increasing complication rates [RR=1.33, 95%CI (1.00, 1.77), P=0.05].

Conclusion: HEN can improve nutritional status, physical function, and fatigue symptoms in post-discharge esophageal cancer patients without increas-

ing gastrointestinal complications, though no significant improvement in overall quality of life was observed.

Keywords: Home Enteral Nutrition; Enteral Tube Feeding; Oral Nutritional Supplements; Nutritional Status; Quality of Life; Meta-Analysis

Introduction

Esophageal cancer ranks as the sixth most common malignancy and the fourth leading cause of cancer-related mortality in China, representing a major public health threat [1]. The prevalence of malnutrition in esophageal cancer patients is the highest among all malignant tumors, reaching 60–85% [2]. Surgical patients are particularly vulnerable, as postoperative gastrointestinal reconstruction leads to malabsorption and further nutritional deterioration [3], which increases complication rates, causes delays or interruptions in chemoradiotherapy, and severely impacts prognosis [4].

While esophageal cancer patients receive adequate nutritional management during hospitalization, their nutritional needs often remain unmet after discharge due to altered dietary patterns following gastrointestinal reconstruction. This frequently results in protein-energy malnutrition [5] and gastrointestinal complications [6-8], which adversely affect treatment response, survival, and quality of life. Since patients remain in recovery phase after discharge, adequate nutrition is crucial for functional recovery and improved quality of life, making post-discharge nutritional support essential.

The benefits of enteral nutrition during hospitalization are well-established, yet the effects of post-discharge enteral support remain understudied. Home enteral nutrition (HEN) refers to the continuation of enteral nutrition support at home under medical supervision for clinically stable patients [9]. Although more patients are receiving HEN, its specific impact on esophageal cancer patients is unclear [10], with inconsistent findings regarding improvements in nutritional status and quality of life, and lingering safety concerns [11-13].

This meta-analysis systematically evaluated the effects of HEN on nutritional status, complications, and quality of life in esophageal cancer patients to provide more robust evidence for clinical practice. Since guidelines consider both enteral tube feeding (ETF) and oral nutritional supplements (ONS) as forms of enteral nutrition described as "nutritional therapy via the enteral route" [14], this study examined both interventions.

Methods

1.1 Inclusion Criteria

(1) Study design: Randomized controlled trials (RCTs) in Chinese or English; (2) Participants: Patients aged $ $18 years with confirmed esophageal cancer who had undergone radical esophagectomy and were discharged; (3) Intervention: HEN support in the experimental group versus regular oral diet in the control group; (4) Primary outcomes: Body weight (BW), body mass index (BMI), hemoglobin (HLB), total protein (TP), albumin (ALB), prealbumin (PAB), transferrin (TRF), malnutrition rate, and complications; Secondary outcomes: Quality of life (QoL).

1.2 Exclusion Criteria

(1) Patients with severe comorbidities such as severe renal impairment or other malignancies; (2) Studies combining HEN with other interventions; (3) Duplicate publications; (4) Studies with unavailable full text, missing data, or incorrect statistical methods; (5) Conference abstracts, letters, and grey literature.

1.3 Search Strategy

We searched PubMed, The Cochrane Library, EMbase, Web of Science, CINHAL, Scopus, Wanfang, CNKI, VIP, and CBM for RCTs on HEN in esophageal cancer patients from database inception to December 2021. The search combined MeSH terms and free-text keywords, adapted for each database, with reference lists of included studies hand-searched for additional sources. Chinese search terms included: esophageal cancer, esophageal malignancy, esophagectomy, home enteral nutrition, jejunostomy, nasogastric feeding, oral nutritional supplements, post-discharge, and home care. English search terms included: esophageal neoplasms, esophageal cancer, esophageal carcinoma, esophagectomy, postesophagectomy, enteral nutrition, tube feeding, oral nutritional supplements, aftercare, discharge, and home. The PubMed search strategy is detailed in Table 1 .

1.4 Study Selection and Data Extraction

Two investigators independently screened literature, extracted data, and cross-checked results, with disagreements resolved through discussion or by a third reviewer. Extracted data included: first author, publication year, sample size, patient age, pathological stage, intervention details, duration, and outcome measures.

1.5 Quality Assessment

Two investigators independently assessed risk of bias using the Cochrane RoB 2.0 tool [15], with results cross-checked.

1.6 Statistical Analysis

Meta-analysis was performed using RevMan 5.4.1. Continuous data were analyzed using standardized mean difference (SMD) or mean difference (MD) with 95% confidence intervals (95%CI). Heterogeneity was assessed using the Q test (α=0.1) and I^2 statistic. If P>0.1 and I^2<50%, a fixed-effects model was used; if P<0.1 and I^2\$ \$50%, sensitivity analysis was performed to identify heterogeneity sources. If heterogeneity persisted, a random-effects model was applied [16]. Subgroup or sensitivity analyses were conducted for significant clinical heterogeneity, or descriptive analysis was performed.

Results

2.1 Literature Search Results

The search yielded 1,210 records. After screening, 22 articles were selected for full-text assessment, with 8 excluded for various reasons. Ultimately, 14 RCTs [11,17-29] were included in the meta-analysis. The screening process is illustrated in Figure 1 [Figure 1: see original paper].

2.2 Characteristics and Risk of Bias of Included Studies

The 14 RCTs published between 2013 and 2021 included 1,040 participants from China (13 studies) and the UK (1 study). The experimental groups received ETF or ONS in addition to oral diet, while control groups received regular oral diet only, with intervention durations of 1–2 months. Study characteristics are summarized in Table 2 .

All studies demonstrated baseline comparability between groups (P>0.05). Nine studies [11,17-20,25,26,28,29] described specific randomization methods, while others only mentioned "random allocation." One study [17] used an online randomization process for allocation concealment, and one [18] used opaque envelopes. Insufficient studies were available for funnel plot analysis to assess publication bias. Risk of bias results are shown in Figure 2 [Figure 2: see original paper].

2.3 Meta-Analysis Results

2.3.1 Effects on Body Weight and BMI Five studies [11,17,20,27,29] assessed BW changes (n=317) with no significant heterogeneity (I^2=5%, P=0.38). Fixed-effects analysis showed significantly less weight loss in the HEN group [SMD=0.63, 95%CI (0.40, 0.85), P<0.00001] (Figure 3 [Figure 3: see original paper]). Eight studies [11,19-21,25-28] assessed BMI changes (n=634) with no heterogeneity (I^2=0%, P=0.57). Fixed-effects analysis showed significantly less BMI decline in the HEN group [SMD=0.60, 95%CI (0.44, 0.76), P<0.00001]

(Figure 4 [Figure 4: see original paper]), indicating HEN effectively prevents weight loss and BMI reduction.

2.3.2 Effects on Serum Nutritional Markers (1) Hemoglobin (HLB) Changes

Seven studies [19,21,23,25-28] assessed HLB changes (n=448) with substantial heterogeneity (I^2=89%, P<0.00001), likely due to intervention type. Five studies [19,23,25,27,28] used jejunostomy tube feeding, while two used other methods. Subgroup analysis of the five jejunostomy studies showed no heterogeneity (I^2=26%, P=0.25). Fixed-effects analysis demonstrated significant HLB improvement [SMD=1.58, 95%CI (1.37, 1.79), P<0.00001] (Figure 5 [Figure 5: see original paper]).

Liu et al. [26] conducted an RCT using duodenal feeding tubes for two months, finding significantly improved HLB levels post-intervention (P<0.05) but no between-group difference (P>0.05). Xueyu Chen et al. [21] used ONS for two months post-discharge, also finding significant HLB improvement (P<0.05) but no between-group difference (P>0.05).

(2) Total Protein (TP) Changes

Eight studies [19,23-29] assessed TP changes (n=690) with substantial heterogeneity (I^2=83%, P<0.00001). Sensitivity analysis did not substantially alter results. Random-effects analysis showed significant TP improvement [SMD=1.19, 95%CI (0.79, 1.58), P<0.00001] (Figure 6 [Figure 6: see original paper]).

(3) Albumin (ALB) Changes

Ten studies [11,19,21,23-29] assessed ALB changes (n=800) with substantial heterogeneity (I^2=84%, P<0.00001), possibly related to intervention type. Eight studies [11,19,23-28] used ETF and two [21,29] used ONS. ETF subgroup analysis showed high heterogeneity (I^2=85%, P<0.00001); random-effects analysis showed significant ALB improvement [SMD=1.25, 95%CI (0.82, 1.68), P<0.00001]. The ONS subgroup showed no heterogeneity (I^2=40%, P=0.20); fixed-effects analysis showed significant ALB improvement [SMD=0.61, 95%CI (0.26, 0.97), P<0.00001] (Figure 7 [Figure 7: see original paper]).

(4) Prealbumin (PAB) Changes

Seven studies [19,21,23-25,28-29] assessed PAB changes (n=560) with no heterogeneity (I^2=0%, P=0.85). Fixed-effects analysis showed significant PAB improvement [SMD=0.97, 95%CI (0.79, 1.14), P<0.00001] (Figure 8 [Figure 8: see original paper]).

(5) Transferrin (TRF) Changes

Four studies [19,23-25] assessed TRF changes (n=351) with substantial heterogeneity (I^2=88%, P<0.0001). Sensitivity analysis did not substantially alter results. Random-effects analysis showed significant TRF improvement

[SMD=1.12, 95%CI (0.45, 1.79), P=0.001] (Figure 9 [Figure 9: see original paper]).

2.3.3 Malnutrition Rate Six studies [11,17,19,22,24,29] assessed malnutrition rates using various scales (NRS-2002, PG-SGA, MNA) (n=566) with no heterogeneity (I^2=36%, P=0.15). Fixed-effects analysis showed significantly reduced malnutrition rates [OR=0.47, 95%CI (0.33, 0.67), P<0.0001] (Figure 10 [Figure 10: see original paper]).

2.3.4 Gastrointestinal Complications Six studies [11,17-19,22,24] assessed gastrointestinal complication rates (n=414) with no heterogeneity (I^2=39%, P=0.15). Fixed-effects analysis showed no significant difference between groups [RR=1.33, 95%CI (1.00, 1.77), P=0.05] (Figure 11 [Figure 11: see original paper]), indicating HEN did not increase complications.

2.3.5 Quality of Life Four studies assessed quality of life (n=168). Meta-analysis of three studies [11,17-18] using the EORTC QLQ-C30 showed no heterogeneity (I^2=5%, P=0.35). Fixed-effects analysis revealed no improvement in overall QoL [MD=4.97, 95%CI (0.06, 9.87), P=0.05] (Figure 12 [Figure 12: see original paper]), but significant improvements in physical function [MD=6.67, 95%CI (2.86, 10.48), P=0.0006] (Figure 13 [Figure 13: see original paper]) and fatigue symptoms [MD=-7.31, 95%CI (-11.85, -2.77), P=0.002] (Figure 14 [Figure 14: see original paper]). Jian Zeng et al. [22] using EORTC QLQ-C18 found higher overall QoL scores in the HEN group at 4 and 12 weeks post-surgery (P<0.05, P<0.01), with better physical, social, and role functioning, less fatigue, and improved weakness, reflux, and appetite, though no difference at 24 weeks.

2.4 Sensitivity Analysis

Sensitivity analysis using the leave-one-out method for all HEN effectiveness measures showed that all pooled results remained statistically significant, indicating robust and stable findings.

Discussion

This meta-analysis of 14 RCTs is the first to evaluate the effects of HEN (including ETF and ONS) on post-discharge esophageal cancer patients after radical esophagectomy. Our findings demonstrate that HEN significantly improves post-discharge body weight, BMI, and serum nutritional markers (ALB, PAB), with comprehensive nutritional assessment showing significantly reduced malnutrition rates. Furthermore, HEN did not increase gastrointestinal complications. While overall QoL was not improved, physical function and fatigue symptoms showed significant enhancement.

Postoperative weight loss is nearly universal in esophageal cancer patients, attributable to altered gastrointestinal anatomy, physiological changes in gut hormones, reduced appetite, and inadequate nutritional intake. After discharge, the direct effects of surgical trauma diminish while malnutrition from gastrointestinal reconstruction becomes the primary concern, serving as an independent risk factor for complications and prognosis [30]. Previous studies indicate approximately 72% of patients achieve only 50-85% of required calories through regular oral diet at discharge [31], while post-discharge ETF can supplement unmet daily requirements and ONS provides more balanced protein and calories than regular diet [18,32]. Our findings confirm that HEN improves post-discharge nutritional status and reduces malnutrition rates.

Heterogeneity in ALB analysis was substantial but sensitivity analysis confirmed robust results, with all studies showing ALB improvement albeit to varying degrees. TRF analysis also showed high heterogeneity, with Cao et al.' s study identified as the source, possibly because patients lacked post-discharge follow-up guidance, leading to imbalanced nutritional intake and minimal TRF improvement. This highlights the importance of post-discharge follow-up.

Gastrointestinal reconstruction alters the type, consistency, and timing of food intake, requiring at least 3-6 months for patients to adapt to new dietary patterns. Most patients experience gastrointestinal complications (reflux, anorexia, diarrhea) within one year post-discharge [33-34], potentially leading to early HEN termination [35]. Therefore, safety assessment is crucial. Our meta-analysis found no significant difference in gastrointestinal complications between groups, likely attributable to professional HEN support teams providing follow-up on dietary intake, physical condition, and complications [19], with dietitians or clinicians monitoring compliance through dietary records and addressing issues via telephone or outpatient visits to prevent complications [11,18]. This underscores the necessity of post-discharge follow-up and the need for improved follow-up protocols.

Quality of life is a critical measure of surgical success, and poor QoL is an independent predictor of mortality [36-37]. Poor QoL in esophageal cancer patients post-surgery is associated with decreased physical function, anorexia, and fatigue [38-40], which can delay chemoradiotherapy and prevent completion of cancer treatment [41-42]. Our analysis showed that while HEN did not improve overall QoL, it significantly enhanced physical function and reduced fatigue. HEN may improve physical vitality through better nutrition, thereby enhancing physical function and alleviating fatigue to facilitate completion of cancer therapy. Cost is another important consideration; our analysis showed no significant difference in the economic impact dimension of EORTC QLQ-C30, suggesting HEN does not increase financial burden, though detailed cost-effectiveness was not reported, warranting further investigation.

Some included studies had methodological limitations that may introduce bias. Additionally, due to reporting limitations, our analysis only compared short-term post-discharge HEN effects, leaving long-term outcomes of ETF and ONS unknown. Finally, most evidence originated from Chinese populations, limiting generalizability to other regions.

Conclusion

Home enteral nutrition effectively improves nutritional status, physical function, and fatigue symptoms in post-discharge esophageal cancer patients without increasing gastrointestinal complications. Healthcare providers should instruct patients on HEN precautions before discharge and ensure adequate follow-up. Further high-quality, large-sample RCTs are needed to provide stronger evidence for HEN implementation in esophageal cancer patients.

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Note: Figure translations are in progress. See original paper for figures.