Postprint of a Meta-Analysis of the Efficacy and Safety of Home Enteral Nutrition in Patients with Esophageal Cancer

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Abstract

Background Esophageal cancer patients frequently experience malnutrition, and studies both domestically and internationally have shown that malnutrition severely impacts patient recovery. Currently, an increasing number of patients are receiving home enteral nutrition (HEN) during home care, but the efficacy and safety of HEN for esophageal cancer patients remain unclear. Objective

To evaluate the efficacy and safety of HEN in esophageal cancer patients through meta-analysis. Methods A computerized search was conducted on PubMed, Cochrane Library, Embase, Web of Science, CINAHL, Scopus, Wanfang Data Knowledge Service Platform, CNKI, VIP, and China Biology Medicine disc to collect randomized controlled trials on esophageal cancer patients receiving HEN, with the search period spanning from database inception to December 2021. Patients in the experimental group received HEN support [including both enteral tube feeding (ETF) and oral nutritional supplements (ONS)], while the control group received only conventional oral diet. Two researchers independently screened literature, extracted data, and assessed study quality using the RoB 2.0 tool recommended by the Cochrane Collaboration. Meta-analysis was performed using RevMan 5.4.1 software. Results A total of 14 studies were included, comprising 1,040 esophageal cancer patients. Meta-analysis results showed that the experimental group had higher increases in body weight (BW), body mass index (BMI), hemoglobin (HLB), serum total protein (TP), serum prealbumin (PAB), and serum transferrin (TRF) compared to the control group [SMD=0.63, 95%CI(0.40,0.85), P<0.00001; SMD=0.60, 95%CI(0.44,0.76), P<0.00001; SMD=1.58, 95%CI(1.37,1.79), P<0.00001; SMD=1.19, 95%CI(0.79,1.58), P<0.00001; SMD=0.97, 95%CI(0.79,1.14), P<0.00001; SMD=1.12, 95%CI(0.45,1.79), P=0.001]. In both the ETF and ONS subgroups, the experimental group showed greater increases in serum albumin (ALB) than the control group [SMD=1.25, 95%CI(0.82,1.68), P<0.00001;

SMD=0.61, 95%CI(0.26,0.97), P<0.00001]. The incidence of malnutrition was lower in the experimental group than in the control group [OR=0.47, 95%CI(0.33,0.67), P<0.0001]. There was no statistically significant difference in the incidence of gastrointestinal complications between the two groups [RR=1.33, 95%CI(1.00,1.77), P=0.05]. No statistically significant difference was observed in quality of life scores between the experimental and control groups [MD=4.97, 95%CI(0.06,9.87), P=0.05]; however, the experimental group had higher physical function scores [MD=6.67, 95%CI(2.86,10.48), P=0.0006] and lower fatigue symptom scores [MD=-7.31, 95%CI(-11.85,-2.77), P=0.002] than the control group. Sensitivity analysis indicated that the pooled results were stable and reliable. Conclusion HEN can improve the nutritional status and physical function of postoperative esophageal cancer patients after hospital discharge, and alleviate their fatigue symptoms, without increasing the incidence of gastrointestinal complications; however, no improvement in overall quality of life was observed.

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 a common complication in patients with esophageal cancer, which seriously impacts patient recovery according to domestic and international studies. While the number of patients receiving home enteral nutrition (HEN) during the home recovery period is increasing, the effectiveness and safety of HEN for esophageal cancer patients remains unclear.

Objective: To systematically evaluate the effectiveness and safety of HEN in esophageal cancer patients through meta-analysis.

Methods: Randomized controlled trials (RCTs) regarding HEN in esophageal cancer patients were retrieved from PubMed, Cochrane Library, Embase, Web of

Science, CINAHL, Scopus, Wanfang Data Knowledge Service Platform, CNKI, VIP, and CBM from inception to December 2021. Patients in the experimental group received HEN support (including both enteral tube feeding [ETF] and oral nutritional supplements [ONS]), while the control group received only conventional oral diet. Two researchers independently screened literature, extracted data, and assessed study quality using the Cochrane Collaboration's RoB 2.0 tool. Meta-analysis was performed using RevMan 5.4.1 software.

Results: Fourteen articles involving 1,040 esophageal cancer patients were included. Meta-analysis showed that the experimental group had significantly greater increases in body weight (BW), body mass index (BMI), hemoglobin (HLB), serum total protein (TP), serum prealbumin (PAB), and serum transferrin (TRF) compared with the control group [SMD=0.63, 95%CI (0.40, 0.85), P<0.00001; SMD=0.60, 95%CI (0.44, 0.76), P<0.00001; SMD=1.58, 95%CI (1.37, 1.79), P<0.00001; SMD=1.19, 95%CI (0.79, 1.58), P<0.00001; SMD=0.97, 95%CI (0.79, 1.14), P<0.00001; SMD=1.12, 95%CI (0.45, 1.79), P=0.001]. In both ETF and ONS subgroups, the experimental group showed greater increases in serum albumin (ALB) than the control group [SMD=1.25, 95%CI (0.82, 1.68), P<0.00001; SMD=0.61, 95%CI (0.26, 0.97), P<0.00001]. The incidence of malnutrition was lower in the experimental group [OR=0.47, 95%CI (0.33, 0.67), P<0.0001]. No statistically significant difference was found in gastrointestinal complication rates between the two groups [RR=1.33, 95%CI (1.00, 1.77), P=0.05]. While overall quality of life scores did not differ significantly between groups [MD=4.97, 95%CI (0.06, 9.87), P=0.05], the experimental group had higher physical function scores [MD=6.67, 95%CI (2.86, 10.48), P=0.0006] and lower fatigue symptom scores [MD=-7.31, 95%CI (-11.85, -2.77), P=0.002]. Sensitivity analysis confirmed the stability and reliability of these results.

Conclusion: HEN can significantly improve nutritional status and physical function while reducing fatigue symptoms in discharged patients after esophageal cancer surgery, without increasing the incidence of gastrointestinal complications. However, no improvement in overall quality of life was observed.

Keywords: Enteral nutrition; Esophageal neoplasms; Home enteral nutrition; Enteral tube feeding; Oral nutritional supplements; Nutritional status; Quality of life; Randomized controlled trial; Meta-analysis

Introduction

Esophageal cancer ranks as the sixth most common malignant tumor and the fourth leading cause of cancer-related mortality in China, representing a major threat to public health [1]. The incidence of malnutrition among esophageal cancer patients is the highest among all malignancies, reaching 60%-85% [2]. For surgical patients in particular, postoperative digestive tract reconstruction leads to malabsorption, further deteriorating nutritional status [3], increasing

complication rates, causing delays or interruptions in chemoradiotherapy, and severely affecting prognosis [4].

While esophageal cancer patients receive adequate nutritional management during hospitalization, they struggle to maintain reasonable nutrient intake after discharge due to altered dietary patterns from digestive tract reconstruction, leading to protein-energy malnutrition [5] and gastrointestinal complications [6-8]. Malnutrition and complications severely impact treatment response, survival time, and quality of life. Therefore, nutritional support after discharge is critically important. Although the benefits of enteral nutrition support during hospitalization are well established, the effects of post-discharge enteral nutrition remain understudied.

Home enteral nutrition (HEN) refers to the continuation of enteral nutrition support at home under medical guidance for clinically stable patients requiring such intervention [9]. With increasing numbers of patients receiving HEN during the home recovery period, its specific impact on esophageal cancer patients remains unclear [10]. Current studies report inconsistent conclusions regarding HEN's effects on nutritional status and quality of life, and safety concerns persist [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 reliable evidence for clinical application. Since guidelines consider both enteral tube feeding (ETF) and oral nutritional supplements (ONS) as forms of enteral nutrition described as "nutritional therapy via enteral routes" [14], this study examined both modalities.

Methods

1.1 Inclusion Criteria

(1) Study type: Randomized controlled trials (RCTs) in Chinese or English; (2) Participants: Patients aged $ $18 years with confirmed esophageal cancer diagnosis who had undergone radical esophagectomy and were discharged; (3) Intervention: Experimental group received HEN support (both ETF and ONS acceptable), while control group received only conventional oral diet; (4) Primary outcomes: Body weight (BW), body mass index (BMI), hemoglobin (HLB), serum total protein (TP), serum albumin (ALB), serum prealbumin (PAB), serum transferrin (TRF), malnutrition incidence, and related complications; Secondary outcome: Quality of life.

1.2 Exclusion Criteria

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

1.3 Search Strategy Computerized searches were conducted in PubMed, Cochrane Library, Embase, Web of Science, CINAHL, Scopus, Wanfang Data Knowledge Service Platform, CNKI, VIP, and CBM from inception to December 2021. Searches combined MeSH terms and free-text words, adjusted according to database characteristics. References of included studies were also searched for additional relevant literature. Chinese search terms included: esophageal cancer, esophageal malignancy, esophagectomy, home enteral nutrition, jejunostomy, nasogastric feeding, oral nutritional supplements, post-discharge, home care. English search terms included: esophageal neoplasms, esophageal cancer, esophageal carcinoma, esophagectomy, postesophagectomy, enteral nutrition, tube feeding, oral nutritional supplements, aftercare, discharge, home. The specific search strategy for PubMed is shown in Table 1 .

1.4 Literature Screening and Data Extraction Two researchers independently screened literature, extracted data, and cross-checked results. Disagreements were resolved through discussion or consultation with a third party. Extracted data included: first author, publication year, sample size, patient age, pathological stage, intervention measures, intervention duration, and outcome indicators.

1.5 Quality Assessment Two researchers independently assessed the risk of bias in included studies using the Cochrane Collaboration's RoB 2.0 tool [15], with results cross-checked.

1.6 Statistical Analysis Meta-analysis was performed using RevMan 5.4.1 software. For continuous data, standardized mean difference (SMD) or mean difference (MD) served as effect measures; for categorical data, odds ratio (OR) or risk ratio (RR) were used, all reported 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%, indicating no significant heterogeneity, 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 analysis was conducted for studies with obvious clinical heterogeneity. Statistical significance was set at P<0.05.

Results

2.1 Literature Search Results The initial search yielded 1,280 records. After screening, 14 articles [11,17-29] were included. The literature screening process is shown in Figure 1 [Figure 1: see original paper].

2.2 Characteristics and Risk of Bias of Included Studies Fourteen RCTs published between 2013-2021 were included, conducted in China [11,18-29] and the United Kingdom [17], totaling 1,040 participants. The intervention

groups received ETF or ONS in addition to oral diet, while control groups received only conventional oral diet, with intervention durations of 1-2 months. Basic characteristics are summarized in Table 2 . All studies showed comparable baselines 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 web-based randomization for allocation concealment, and one [18] used opaque envelopes. Risk of bias assessment is shown in Figure 2 [Figure 2: see original paper].

2.3 Effects of HEN

2.3.1 Effects on BW and BMI Five studies [11,17,20,27,29] examined BW changes (n=317) with no significant heterogeneity (I^2=5%, P=0.38). Fixed-effects model analysis showed greater BW gain in the intervention 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] examined BMI changes (n=634) with no heterogeneity (I^2=0%, P=0.57), showing greater BMI gain in the intervention group [SMD=0.60, 95%CI (0.44, 0.76), P<0.00001, Figure 4 [Figure 4: see original paper]].

2.3.2 Effects on Serum Nutritional Markers 2.3.2.1 HLB Changes: Seven studies [19,21,23,25-28] examined HLB changes (n=448) with substantial heterogeneity (I^2=89%, P<0.00001), likely due to intervention type differences. Five studies [19,23,25,27-28] used jejunostomy feeding, one [26] used duodenal feeding, and one [21] used ONS. Meta-analysis of the five jejunostomy studies (I^2=26%, P=0.25) showed significantly greater HLB increase in the intervention group [SMD=1.58, 95%CI (1.37, 1.79), P<0.00001, Figure 5 [Figure 5: see original paper]]. The remaining two studies were analyzed descriptively.

LIU XJ [26] conducted an RCT on duodenal feeding for 2 months, finding significantly improved HLB levels post-intervention (P<0.05) but no between-group difference (P>0.05). CHEN et al. [21] provided ONS for 2 months post-discharge, also finding significant HLB improvement (P<0.05) but no between-group difference (P>0.05).

2.3.2.2 TP Changes: Eight studies [19,23-29] examined TP changes (n=690) with substantial heterogeneity (I^2=83%, P<0.00001). Random-effects analysis showed greater TP increase in the intervention group [SMD=1.19, 95%CI (0.79, 1.58), P<0.00001, Figure 6 [Figure 6: see original paper]].

2.3.2.3 ALB Changes: Ten studies [11,19,21,23-29] examined ALB changes (n=800) with substantial heterogeneity (I^2=84%, P<0.00001), likely due to intervention type. Eight studies [11,19,23-28] used ETF and two [21,29] used ONS, prompting subgroup analysis. The ETF subgroup (I^2=85%, P<0.00001) showed greater ALB increase with random-effects model [SMD=1.25, 95%CI (0.82, 1.68), P<0.00001, Figure 7 [Figure 7: see original paper]]. The ONS sub-

group (I^2=40%, P=0.20) showed greater ALB increase with fixed-effects model [SMD=0.61, 95%CI (0.26, 0.97), P<0.00001, Figure 7].

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

2.3.2.5 TRF Changes: Four studies [19,23-25] examined TRF changes (n=351) with substantial heterogeneity (I^2=88%, P<0.0001). Sensitivity analysis did not substantially change results. Random-effects analysis showed greater TRF increase in the intervention group [SMD=1.12, 95%CI (0.45, 1.79), P=0.001, Figure 9 [Figure 9: see original paper]].

2.3.3 Effects on Malnutrition Seven studies [19,21-23,25,26,28] examined the proportion of patients at nutritional risk or with malnutrition using various assessment tools (NRS 2002, PG-SGA, MNA) (n=566) with no heterogeneity (I^2=36%, P=0.15). Fixed-effects analysis showed lower malnutrition incidence in the intervention group [OR=0.47, 95%CI (0.33, 0.67), P<0.0001, Figure 10 [Figure 10: see original paper]].

2.3.4 Effects on Gastrointestinal Complications Six studies [11,17-19,22,24] examined 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]].

2.3.5 Effects on Quality of Life Four studies [11,17-18,22] assessed quality of life (n=168). Three studies [11,17,18] using EORTC QLQ-C30 were meta-analyzed, while one [22] using EORTC QLQ-C18 was descriptively analyzed. The three studies showed no heterogeneity (I^2=5%, P=0.35). Fixed-effects analysis revealed no significant difference in overall quality of life [MD=4.97, 95%CI (0.06, 9.87), P=0.05, Figure 12 [Figure 12: see original paper]], but higher physical function scores [MD=6.67, 95%CI (2.86, 10.48), P=0.0006, Figure 13 [Figure 13: see original paper]] and lower fatigue symptom scores [MD=-7.31, 95%CI (-11.85, -2.77), P=0.002, Figure 14 [Figure 14: see original paper]] in the intervention group.

ZENG et al. [22] reported higher overall quality of life scores in the intervention group at 4 and 12 weeks post-surgery (P<0.05), with better performance in physical, social, and role functions, lower fatigue scores, and superior outcomes in weakness, reflux, and appetite. No significant difference was found at 24 weeks.

Discussion

This meta-analysis demonstrates that HEN effectively improves nutritional status and physical function while reducing fatigue symptoms in discharged esophageal cancer patients post-surgery, without increasing gastrointestinal complications. However, no improvement in overall quality of life was observed.

Postoperative weight loss is nearly universal in esophageal cancer patients, attributable to altered digestive anatomy, physiological changes in gastrointestinal hormones, reduced appetite, and inadequate nutritional intake. After discharge, while direct surgical trauma effects wane, malnutrition from digestive reconstruction becomes the primary issue, serving as an independent risk factor for complications and prognosis [30]. Previous research indicates approximately 72% of patients achieve only 50%-85% of required calories through conventional oral diet at discharge [31], while post-discharge ETF can supplement unmet daily needs, and ONS provides more balanced protein and calories than regular diet [18,32], thereby improving nutritional status.

This study found HEN significantly improved post-discharge BW, BMI, and serum nutritional markers (ALB, PAB) while reducing malnutrition incidence. Substantial heterogeneity in ALB analysis was robust upon sensitivity analysis, with all studies showing improvement albeit to varying degrees. TRF analysis also showed substantial heterogeneity, with CAO et al. [24] identified as the source—likely because patients lacked post-discharge medical follow-up guidance, leading to unbalanced nutritional intake and minimal TRF improvement. This highlights the necessity of post-discharge follow-up.

Due to digestive reconstruction, patients require 3-6 months to adapt to new dietary patterns, yet most 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. This 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 essential nature of post-discharge follow-up.

Quality of life is a critical surgical outcome measure, with poor quality of life being an independent mortality risk factor [36-37]. Post-esophagectomy quality of life is associated with decreased physical function, anorexia, and fatigue [38-40], which can delay chemoradiotherapy and compromise complete cancer treatment [41-42]. HEN may improve physical function and reduce fatigue by providing adequate nutrition, thereby enhancing vitality and helping patients complete treatment. Cost is another important consideration; this analysis found no significant difference in economic impact on the EORTC QLQ-C30, suggesting HEN does not increase financial burden, though detailed cost-effectiveness reporting was lacking, warranting further exploration.

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

In conclusion, HEN effectively improves nutritional status, physical function, and fatigue symptoms in discharged esophageal cancer patients without increasing gastrointestinal complications. Clinicians should provide HEN guidance before discharge and ensure adequate follow-up. Further high-quality, large-sample RCTs are needed to strengthen the evidence base for HEN implementation in esophageal cancer patients.

Author Contributions: XUE Shan conceived the study, conducted literature review, and drafted the manuscript; LIANG Junli performed data analysis and interpretation; JIN Yinghui provided overall supervision; WEI Shuyan provided guidance and critical review; LI Laiyou oversaw feasibility, quality control, and critical revision.

Conflict of Interest: None declared.

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