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ORIGINAL ARTICLE – GASTROINTESTINAL ONCOLOGY

# A Prospective Randomized Trial of Enteral Nutrition After Thoracoscopic Esophagectomy for Esophageal Cancer

Tomoko Takesue, MD, Hiroya Takeuchi, MD, PhD, FACS, Masaharu Ogura, MD, PhD, Kazumasa Fukuda, PhD, Rieko Nakamura, MD, PhD, Tsunehiro Takahashi, MD, PhD, Norihito Wada, MD, PhD, Hirofumi Kawakubo, MD, PhD, and Yuko Kitagawa, MD, PhD

Department of Surgery, Keio University School of Medicine, Tokyo, Japan

## ABSTRACT

**Background.** Several studies have reported that postoperative enteral nutrition (EN) reduced complications and decreased weight loss and hospital stay periods; however, the majority of patients analyzed in these studies underwent open thoracic surgery. No studies have been conducted regarding EN in patients after thoracoscopic esophagectomy as a less invasive surgery. The aim of this study was to investigate the efficacy of EN after thoracoscopic esophagectomy.

**Methods.** Fifty patients who underwent thoracoscopic esophagectomy for esophageal cancer were divided into two groups: parenteral nutrition (PN; $n = 25$) and EN ($n = 25$). The rate of weight loss at postoperative day (POD) 14, levels of prealbumin at POD 10, postoperative complications until POD 14, and other perioperative data were collected for each group.

**Results.** This study analyzed data for 47 patients. The rate of weight loss at POD 14 was significantly lower in the EN group ($3.0 \pm 3.2$ %) than in the PN group ($4.0 \pm 3.6$ %; $p = 0.020$). Prealbumin levels were $21.0 \pm 7.5$ mg/dL in the PN group and $18.4 \pm 5.8$ mg/dL in the EN group at POD 10, with no significant differences between the groups. However, the incidence of postoperative pneumonia was higher in the PN group (30.4 %) than in the EN group (12.5 %).

**Conclusions.** EN could suppress weight loss and reduce the incidence of pneumonia after thoracoscopic esophagectomy.

Esophageal cancer is a highly aggressive malignancy that metastasizes to the lymph nodes and is associated with a poor prognosis. The 5-year overall survival rate is 40.0 % and the 30-day mortality rate is 1.7 %0.[1] Surgical resection is the most effective treatment for localized esophageal cancer; however, esophagectomy is extremely invasive and is associated with high morbidity and mortality rates.

Thoracoscopic esophagectomy for esophageal cancer was first reported by Cuschieri et al.[2] in 1992 and has been increasingly adopted as a minimally invasive esophagectomy. A current review of thoracoscopic esophagectomy showed that single-institution studies and several meta-analyses have demonstrated acceptable short-term outcomes compared with open esophagectomy.[3] The first multicenter trial comparing thoracoscopic esophagectomy and open esophagectomy [TIME trial (Traditional Invasive vs. Minimally invasive Esophagectomy)] reported that the incidence of postoperative pulmonary infection was markedly lower in the thoracoscopic group. Additional benefits of thoracoscopic esophagectomy in this trial were less operative blood loss, better postoperative quality of life for patients, and shorter hospital stay.[4]

Nutrition is one of the most important factors to consider after esophagectomy in order to reduce surgical mortality.[5,6] The European Society for Parenteral and Enteral Nutrition guidelines recommend early tube feeding after major gastrointestinal surgery for cancer.[7] Several studies have shown that enteral nutrition (EN) is more effective than parenteral nutrition (PN) in reducing postoperative complications in postesophagectomy patients;[8–10] however, these studies mainly analyzed patients who underwent open esophagectomy. No studies have been conducted showing the efficacy of EN in patients after thoracoscopic esophagectomy.

We hypothesized that EN was also recommended after thoracoscopic esophagectomy in esophageal cancer

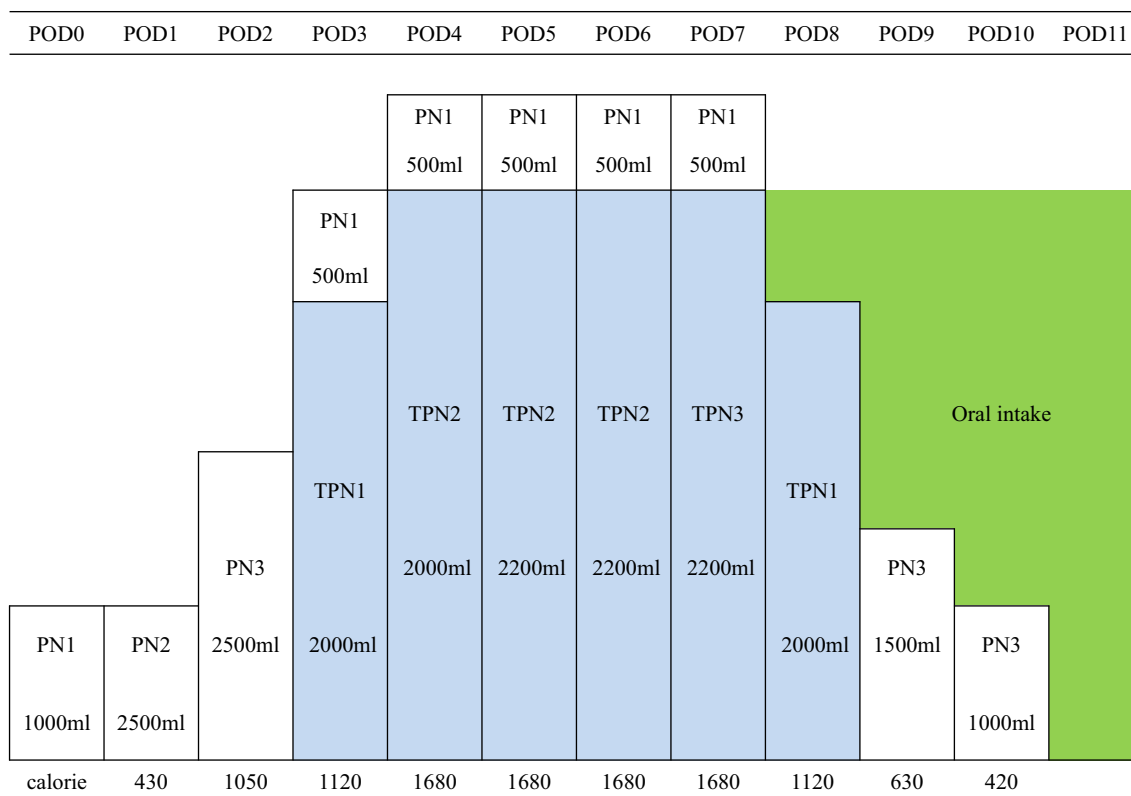| | POD0 | POD1 | POD2 | POD3 | POD4 | POD5 | POD6 | POD7 | POD8 | POD9 | POD10 | POD11 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | PN1 500ml | PN1 500ml | PN1 500ml | PN1 500ml | PN1 500ml | | | | |
| | | | PN3 2500ml | TPN1 2000ml | TPN2 2000ml | TPN2 2200ml | TPN2 2200ml | TPN3 2200ml | TPN1 2000ml | PN3 1500ml | PN3 1000ml | Oral intake |
| | PN1 1000ml | PN2 2500ml | | | | | | | | | | |
| calorie | 430 | 1050 | 1120 | 1680 | 1680 | 1680 | 1680 | 1120 | 630 | 420 | | |

FIG. 1 Protocol for parenteral nutrition. PN1: sodium 130 mEq/L, potassium 4 mEq/L, calcium 3 mEq/L, chlorine 109 mEq/L, lactate 28 mEq/L, glucose 0 g/L, calories 0 kcal/L; PN2: sodium 35 mEq/L, potassium 20 mEq/L, chlorine 35 mEq/L, lactate 20 mEq/L, glucose 43 g/L, calories 172/L; PN3: sodium 35 mEq/L, potassium 20 mEq/L, magnesium 5 mEq/L, calcium 5 mEq/L, chlorine 35 mEq/L, sulfate 5 mEq/L, lactate 20 mEq/L, acetate 16 mEq/L, glucose 75 g/L, free amino acid 30 g/L, thiamine 1.5 mg, calories 420/L; TPN1: sodium 50 mEq/L, potassium 22 mEq/L, magnesium 4 mEq/L, calcium 4 mEq/L, chlorine 50 mEq/L, sulfate 4 mEq/L, lactate 12 mEq/L, acetate 41 mEq/L, glucose 120 g/L, free amino acid 20 g/L, calories 560/L; TPN2: sodium 50 mEq/L, potassium 27 mEq/L, magnesium 5 mEq/L, calcium 5 mEq/L, chlorine 50 mEq/L, sulfate 5 mEq/L, lactate 15 mEq/L, acetate 50 mEq/L, glucose 175 g/L, free amino acid 30 g/L, calories 820/L. *POD* postoperative day

patients. In this study, we conducted a randomized controlled trial comparing PN and EN after thoracoscopic esophagectomy.

## MATERIALS AND METHODS

After thoracoscopic esophagectomy for esophageal cancer, patients were randomly divided into the PN and EN groups and treated as per each study protocol. The medical data of the patients were prospectively collected. The primary endpoint was the rate of weight loss at postoperative day (POD) 14 from preoperative weight, while secondary endpoints were serum prealbumin levels at POD 10 and postoperative complications until POD 14.

Patient selection criteria were (i) patients undergoing planned thoracoscopic esophagectomy with two- or three-field lymphadenectomy at Keio University Hospital, Tokyo, Japan; (ii) patient consent to participate in this study; (iii) age 20–75 years; (iv) body mass index (BMI) 18–25 kg/m$^2$; and (v) an American Society of Anesthesiologists physical status of I or II. Exclusion criteria were severe ischemic heart disease, cerebrovascular disease, chronic renal failure (creatinine clearance rate $<30$ mL/min), severe diabetes, liver dysfunction, severe obesity (BMI $>25$ kg/m$^2$), severe emaciation (BMI $<18$ kg/m$^2$), amino acid metabolism disorder, pregnancy, and preoperative chemoradiation therapy.

Patients in the PN group received total PN from a central venous catheter, as per the study protocol (Fig. 1), and patients in the EN group underwent jejunostomy during esophagectomy, and commenced 24-h continuous jejunostomy feeding of an elemental diet immediately after surgery. According to the study protocol (Fig. 2), the initial dose of the enteral diet was 10 mL/h, gradually increasing to 70 mL/h. Two study protocols were designed to comprise almost identical total calories and total moisture content.

Although patients essentially received nutrition as per either protocol, in both groups, the quantity of infusion solutions or enteral feeding solutions was changed depending on the patient's condition. For example, an additional transfusion to improve dehydration or a

reduction in enteral solution due to diarrhea was included. Total intake quantity and total calories were retrospectively calculated for each patient.

All patients consumed an enteral diet of 400 mL/day orally for 5 days prior to surgery. A peripherally inserted central catheter was inserted from the arm before surgery, and hydrocortisone (200 mg/day) was administered for 5 days—2 days before and 3 days after surgery.

During surgery, the thoracic procedure was performed by video-assisted thoracoscopic surgery, and the abdominal procedure was performed by open laparotomy or hand-assisted laparoscopic surgery (HALS), as previously described.[11] Fields of lymph node dissection and thoracic duct resection were decided according to the tumor progression and preoperative risk of each patient. A single surgical team including three operators performed all the thoracoscopic esophagectomies, in which two of the three surgeons always participated as assistants.

After surgery, patients were treated with an artificial ventilator in the intensive care unit (ICU), until POD 1. Patients routinely underwent computed tomography (CT) scans to detect postoperative complications on POD 6, and contrast imaging to check swallowing functions on POD 7. As a result of the CT scan and swallowing examination, patients without severe complications started oral intake on POD 8. Thereafter, the quantity of infusion solutions or enteral feeding solutions was decreased depending on oral intake. Patients who recovered well were discharged after POD 14. Blood sugar levels were measured four times a day in all patients, and insulin was injected or mixed into infusion solutions, depending on these levels.

Collected postoperative data included weight at POD 14, prealbumin level at POD 10, postoperative complications until POD 14, oral intake commencement day, ICU stay and postoperative hospital-stay durations, total intake (infusion solution and enteral diet) and discharge (urine and drain discharge) quantities until POD 14, and postoperative blood test results [total protein, albumin, total bilirubin, aspartate transaminase, alanine aminotransferase, blood sugar, C-reactive protein (CRP) levels, white blood cell (WBC) and platelet counts, and prothrombin time]. Postoperative complications were diagnosed using X-ray, computed tomography, and clinical features, and the severity of complications was classified using the Clavien–Dindo classification grade of surgical complications.[12]

Statistical analyses between the groups were performed using the Mann–Whitney $U$ test and Chi square test using IBM SPSS statistical software version 22 (IBM Corporation, Armonk, NY, USA). A probability ($p$) value of $<0.05$ was considered statistically significant.

Sample size was determined on the basis of our previous postoperative data of 52 patients administered EN or PN after esophagectomy during 2006–2009. The mean rate of weight loss from preoperative weight at POD 14 was 6.0 % in the EN group and 7.5 % in the PN group. Calculated sample size for which 80 % statistical power could be expected was 34 patients (17 patients/group), on the assumption that the standard deviation was 5 and mean weight loss rate improved by 5 % using EN. The sample size of this study was determined as 50 patients (25 patients/group) to allow for accidental errors.

The study protocol was approved by the Ethics Committee of Keio University School of Medicine (UMIN000014884), and written informed consent was obtained from all patients in the study.

## RESULTS

### Patient Characteristics

Fifty patients were enrolled in this study from March 2012 to July 2014, and the data of 47 patients were analyzed. Three patients were excluded from analysis because the surgery was converted to open surgery in one patient, one patient in the PN group received enteral feeding because of severe anastomotic leakage, and one patient in the EN group received only PN because of additional surgery (colectomy) for another disease.

Patient characteristics are shown in Table 1. The 47 patients analyzed comprised 37 (78.8 %) men and 10 (21.2 %) women, with a mean age of 62.2 years (range 46–74). There were no significant differences in age, sex, height, weight, medical history, preoperative blood test results, neoadjuvant chemotherapy, or pathological TNM classification (UICC TNM Classification of Malignant Tumors, 7th edition).

### Surgical Procedures

Intraoperative data are summarized in Table 2. The abdominal procedure was performed with HALS in 46 (97.9 %) patients. Forty-three (95.7 %) patients underwent three-field lymph node dissection and 45 (95.7 %) patients underwent thoracic duct resection. Mean surgical duration was $556 \pm 52$ min and mean blood loss was $208 \pm 139$ mL. No significant differences in the surgical procedure between the two groups were observed.

### Primary and Secondary Endpoint

The results of primary and secondary endpoints are shown in Table 3. The mean rate of weight loss for all patients at POD 14 was $4.0 \pm 3.6$: $5.1 \pm 3.7$ % in the PN group and $3.0 \pm 3.2$ % in the EN group. Weight loss after

**TABLE 1** Characteristics of patients

| | All patients (n = 47) | | Parenteral nutrition (n = 23) | | Enteral nutrition (n = 24) | | p value |
|---|---|---|---|---|---|---|---|
| Age (years) | 62.2 ± 8.12 | | 60.7 ± 8.97 | | 63.6 ± 7.13 | | 0.281 |
| Sex (M/F) | 37/10 | | 18/5 | | 19/5 | | 0.940 |
| Height (m) | 1.66 ± 0.10 | | 1.66 ± 0.12 | | 1.66 ± 0.06 | | 0.790 |
| Weight (kg) | 59.8 ± 11.9 | | 57.2 ± 12.1 | | 62.3 ± 11.3 | | 0.225 |
| Medical history [n (%)] | | | | | | | |
|   Hypertension | 13 (27.7) | | 4 (17.4) | | 9 (37.5) | | 0.127 |
|   Diabetes mellitus | 5 (10.6) | | 1 (4.3) | | 4 (16.7) | | 0.176 |
|   Malignant tumor | 3 (6.4) | | 1 (4.3) | | 2 (8.3) | | 0.580 |
|   Hyperlipidemia | 3 (6.4) | | 0 (0.0) | | 3 (12.5) | | 0.083 |
|   Gastric ulcer | 3 (6.4) | | 3 (13.0) | | 0 (0.0) | | 0.070 |
|   Hepatitis | 2 (4.3) | | 1 (4.3) | | 1 (4.2) | | 0.976 |
|   COPD | 1 (2.1) | | 1 (4.3) | | 0 (0.0) | | 0.307 |
|   Others | 5 (10.6) | | 2 (8.7) | | 3 (12.5) | | 0.676 |
| Preoperative blood test | | | | | | | |
|   Total protein (g/dL) | 6.4 ± 0.4 | | 6.4 ± 0.4 | | 6.4 ± 0.5 | | 0.923 |
|   Albumin (g/dL) | 4.0 ± 0.4 | | 4.1 ± 0.2 | | 4.0 ± 0.4 | | 0.708 |
|   Total bilirubin (mg/dL) | 0.7 ± 0.2 | | 0.7 ± 0.2 | | 0.7 ± 0.3 | | 0.400 |
|   AST (U/L) | 23 ± 10 | | 21 ± 8.1 | | 24 ± 11 | | 0.281 |
|   ALT (U/L) | 20 ± 17 | | 17 ± 13 | | 23 ± 19 | | 0.141 |
|   HbA1c (%) | 5.8 ± 0.6 | | 5.8 ± 0.5 | | 5.8 ± 0.8 | | 0.543 |
|   CRP (mg/dL) | 0.11 ± 0.21 | | 0.13 ± 0.26 | | 0.09 ± 0.14 | | 0.889 |
|   WBC ($\times 10^3/\mu$L) | 6.4 ± 2.2 | | 6.6 ± 2.4 | | 6.3 ± 2.1 | | 0.709 |
|   Plt ($\times 10^4/\mu$L) | 22.9 ± 6.2 | | 23.5 ± 5.7 | | 22.3 ± 6.7 | | 0.273 |
|   Prothrombin time (%) | 96.4 ± 7.7 | | 97.7 ± 6.1 | | 95.2 ± 9.0 | | 0.211 |
| Preoperative therapy [n (%)] | | | | | | | |
|   Chemotherapy | 25 | (53.2) | 13 | (56.5) | 12 | (50.0) | 0.658 |
| TNM classification (UICC 7th edition) [n (%)] | | | | | | | |
|   Primary tumor | | | | | | | 0.643 |
|     pT1 | 34 | (72.3) | 16 | (69.6) | 18 | (75.0) | |
|     pT2 | 4 | (8.5) | 3 | (13.0) | 1 | (4.2) | |
|     pT3 | 9 | (19.1) | 4 | (17.4) | 5 | (20.8) | |
|   Resional lymph node | | | | | | | 0.493 |
|     pN0 | 25 | (53.2) | 13 | (56.5) | 12 | (50.0) | |
|     pN1 | 16 | (34.0) | 8 | (34.8) | 8 | (33.3) | |
|     pN2 | 3 | (6.4) | 2 | (8.7) | 1 | (4.2) | |
|     pN3 | 3 | (6.4) | 0 | (0.0) | 3 | (12.5) | |
|   Distant metastasis | | | | | | | 0.418 |
|     pM0 | 41 | (87.2) | 21 | (91.3) | 20 | (83.3) | |
|     pM1 (lymph node metastasis) | 6 | (12.8) | 2 | (8.7) | 4 | (16.7) | |
| Stage | | | | | | | 0.469 |
|   I | 21 | (44.7) | 11 | (47.8) | 10 | (41.7) | |
|   II | 13 | (27.7) | 7 | (30.4) | 6 | (25.0) | |
|   III | 7 | (14.9) | 3 | (13.0) | 4 | (16.7) | |
|   IV | 6 | (12.8) | 2 | (8.7) | 4 | (16.7) | |

*COPD* chronic obstructive pulmonary disease, *AST* aspartate transaminase, *ALT* alanine aminotransferase, *CRP* C-reactive protein, *WBC* white blood cell, *M* male, *F* female, *UICC* Union for International Cancer Control, ± indicates mean ± SD

**TABLE 2** Intraoperative data

| | All patients ($n = 25$) | Parenteral nutrition ($n = 23$) | Enteral nutrition ($n = 24$) | $p$-Value |
|---|---|---|---|---|
| Surgical procedure [$n$ (%)] | | | | |
| Hand-assisted laparoscopic surgery | 46 (97.9) | 23 (100) | 23 (95.8) | 0.328 |
| Lymph node dissection | | | | |
| Two-fields | 4 (8.5) | 1 (4.3) | 3 (12.5) | 0.322 |
| Three-fields | 43 (91.5) | 22 (95.7) | 21 (87.5) | |
| Number of dissected lymph nodes (mean ± SD) | 72 ± 23 | 67 ± 26 | 77 ± 19 | 0.053 |
| Thoracic duct resection [$n$ (%)] | 45 (95.7) | 22 (95.6) | 23 (95.8) | 0.976 |
| Operation time (min; mean ± SD) | 556 ± 52 | 548 ± 53 | 564.2 ± 51.2 | 0.395 |
| Blood loss (mL; mean ± SD) | 208 ± 139 | 211 ± 122 | 207 ± 157 | 0.616 |
| Blood transfusion (mL; mean ± SD) | 88 ± 222 | 36 ± 128 | 137 ± 279 | 0.263 |
| Albumin solution (mL; mean ± SD) | 1044 ± 299 | 989 ± 324 | 1097 ± 269 | 0.155 |

*SD* standard deviation

surgery was significantly prevented in the EN group ($p = 0.020$).

Mean prealbumin level was $19.7 \pm 6.8$ mg/dL at POD 10: $21.0 \pm 7.5$ mg/dL in the PN group and $18.4 \pm 5.8$ mg/dL in the EN group. No significant differences were observed between the groups ($p = 0.257$).

Postoperative complications occurred in 34 (72.3 %) of 47 patients. Severe complications (Clavien–Dindo grade 3 or higher) occurred in eight (17.0 %) patients: four with recurrent nerve paralysis, three with pneumonia, one with cerebral hemorrhage, and one with thoracic emphysema. No significant differences were observed between groups for all complications ($p = 0.680$), each complication, or severe complications ($p = 0.137$). However, the incidence of pneumonia was higher in the PN group (30.4 %, seven patients) than in the EN group (12.5 %, three patients). One patient in each group had a catheter-associated infection. In the EN group, no severe complication relating to enteral feeding, such as peritonitis, ileus, or severe diarrhea, was observed. In both groups, the postoperative mortality rate was 0 %.

*Postoperative Data*

Postoperative data are shown in Table 3. Mean ICU stay was 2.7 days in both groups ($p = 0.327$). The mean PODs of oral intake commencement were $13.9 \pm 7.7$ in the PN group and $15.1 \pm 9.5$ in the EN group ($p = 0.664$). Postoperative hospital stay was longer in the EN group ($30.5 \pm 9.0$ days) than in the PN group ($27.8 \pm 14.3$ days). No differences were observed in durations of ICU stay, oral intake, and hospital stay ($p = 0.327$, $p = 0.664$, and $p = 0.058$, respectively).

Postoperative blood test results were almost identical in the two groups. No significant differences ($p = 0.912$) were observed in the mean values of blood sugar levels during the 10-day period after surgery—$155.2 \pm 21.3$ mg/dL in the PN group and $159.7 \pm 28.6$ mg/dL in the EN group.

During the 7-day period after surgery, no differences in the mean values of intake (infusion solution and enteral diet) and calories were observed. However, the mean amount of discharge (urine and drain discharge) was significantly larger in the PN group (2.9 L/day) than in the EN group (2.5 L/day) ($p = 0.011$).

Five patients in the EN group required enteral feeding to be continued after discharge from hospital in order to support their nutrition. Two patients in the PN group, complicated by cerebral hemorrhage or severe recurrent laryngeal nerve paralysis, required enteral feeding, using a nasojejunal tube, on POD 17 and POD 28.

## DISCUSSION

To the best of our knowledge, this is the first prospective randomized study of early EN after thoracoscopic esophagectomy. The results of this study demonstrated that postoperative EN suppressed weight loss at POD 14. The incidence of pneumonia tended to be lower in the PN group than in the EN group, and no significant differences were observed in serum levels of prealbumin, or incidence of complications, between the PN and EN groups.

Several studies have advocated that after esophagectomy, postoperative EN reduces the incidence of complications,[8–10] duration of ICU stay,[13] duration of hospital stay,[9,13] and postoperative weight loss.[14] Early recovery of the total WBC count and decrease in the serum levels of total bilirubin and CRP in patients with early EN have also been reported.[15]

In this study, weight loss after surgery was significantly prevented in the EN group. Although no differences in administered calories or moisture content were observed, the amount of discharge until POD 7 was significantly

**TABLE 3** Postoperative data

| | All patients (n = 47) | Parenteral nutrition (n = 23) | Enteral nutrition (n = 24) | p-Value |
|---|---|---|---|---|
| Primary endpoint | | | | |
| Rate of weight loss at 14 POD (%; mean ± SD) | 4.00 ± 3.56 | 5.05 ± 3.65 | 2.94 ± 3.19 | 0.020 |
| Secondary endpoint | | | | |
| Prealbumin at 10 POD (mg/dL; mean ± SD) | 19.7 ± 6.77 | 21.0 ± 7.48 | 18.4 ± 5.82 | 0.257 |
| Complications [n (%)] | | | | |
| Recurrent laryngeal nerve paralysis | 13 (27.7) | 6 (26.1) | 7 (29.2) | 0.815 |
| Pneumonia | 10 (21.3) | 7 (30.4) | 3 (12.5) | 0.137 |
| Anastomotic leakage | 8 (17.0) | 4 (17.4) | 5 (20.8) | 0.767 |
| Thrombosis | 7 (14.9) | 4 (17.4) | 3 (12.5) | 0.641 |
| Atelectasis | 4 (8.5) | 2 (8.7) | 2 (8.3) | 0.965 |
| Lymphorrhea | 4 (8.5) | 2 (8.7) | 2 (8.3) | 0.965 |
| Others | 9 (19.1) | 4 (17.4) | 5 (20.8) | 0.767 |
| Any complications | 34 (72.3) | 16 (69.6) | 18 (75.0) | 0.680 |
| Severe complications | 8 (17.0) | 5 (21.7) | 3 (12.5) | 0.461 |
| Postoperative data (mean ± SD) | | | | |
| Nutrition and balance (until POD 7) | | | | |
| Calories of intake (kcal/day) | 1103.0 ± 273.2 | 1104.3 ± 202.7 | 1101.6 ± 159.0 | 0.483 |
| Intake (mL/day) | 3011.1 ± 322.0 | 2985.2 ± 345.8 | 3036.0 ± 302.7 | 0.407 |
| Discharge (mL/day) | 2708.9 ± 502.4 | 2891.1 ± 481.45 | 2534.3 ± 467.0 | 0.011 |
| Postoperative course | | | | |
| Start of oral intake (POD) | 14.5 ± 8.7 | 13.9 ± 7.7 | 15.1 ± 9.5 | 0.664 |
| ICU stay (days) | 2.7 ± 2.0 | 2.7 ± 2.3 | 2.7 ± 1.6 | 0.327 |
| Postoperative hospital stay (days) | 27.7 ± 11.8 | 27.1 ± 14.7 | 28.3 ± 8.4 | 0.147 |
| Postoperative blood test | | | | |
| Total protein (at POD14; g/dL) | 5.9 ± 0.4 | 6.0 ± 0.4 | 5.9 ± 0.6 | 0.811 |
| Albumin (at POD14; g/dL) | 3.1 ± 0.4 | 3.2 ± 0.3 | 3.1 ± 0.5 | 0.57 |
| Total bilirubin (mg/dL) | 1.7 ± 1.1 | 2.0 ± 1.4 | 1.3 ± 0.7 | 0.079 |
| AST (maximal values; IU/L) | 66.2 ± 43.5 | 58.0 ± 21.1 | 74.1 ± 56.7 | 0.882 |
| ALT (maximal values; IU/L) | 83.8 ± 74.8 | 74.3 ± 45.2 | 92.8 ± 95.3 | 0.717 |
| Blood sugar (mean of 10 days; mg/dL) | 157.5 ± 25.3 | 155.2 ± 21.5 | 159.7 ± 28.6 | 0.912 |
| CRP (maximal values; mg/mL) | 13.4 ± 4.0 | 13.3 ± 4.0 | 13.5 ± 4.1 | 0.406 |
| WBC (maximal values; $\times 10^3$/μL) | 13.4 ± 4.0 | 13.6 ± 4.3 | 13.2 ± 3.8 | 0.595 |
| Platelet (minimal values; $\times 10^4$/μL) | 15.3 ± 4.2 | 15.4 ± 4.5 | 15.3 ± 4.1 | 0.941 |
| Prothrombin time (minimal values; %) | 68.0 ± 11.5 | 71.0 ± 8.5 | 67.0 ± 10.5 | 0.338 |

*AST* aspartate transaminase, *ALT* alanine aminotransferase, *CRP* C-reactive protein, *WBC* white blood cell, *SD* standard deviation, *POD* postoperative day, *ICU* intensive care unit

Thrombosis: pulmonary embolism, deep vein thrombosis, or jugular vein thrombosis

Severe complications: complication diagnosed as Clavien–Dindo grade 3 or higher

smaller in the EN group. In the PN group, more moisture may have been transferred to the third space or urine than in the EN group. EN may also superiorly help in absorbing nutrients and suppressing weight loss compared with PN. However, no differences in prealbumin levels at POD 10 were observed between the two groups. Prealbumin is known as the earliest laboratory indicator of nutritional status.[16] Because prealbumin is also a marker of tissue permeability, it is affected by inflammatory response and steroid use.[17] Prealbumin cannot exactly reflect nutritional status after invasive surgery.

EN and postoperative complications, particularly infectious complications, after gastrointestinal surgery are related.[6,8] Few mechanisms whereby EN reduced postoperative complications have been reported. EN prevents atrophy of gastrointestinal mucosa and inhibits bacterial translocation from the gut to the blood stream.[18] It reduces sequestration of the fluid in the third space and improves pulmonary
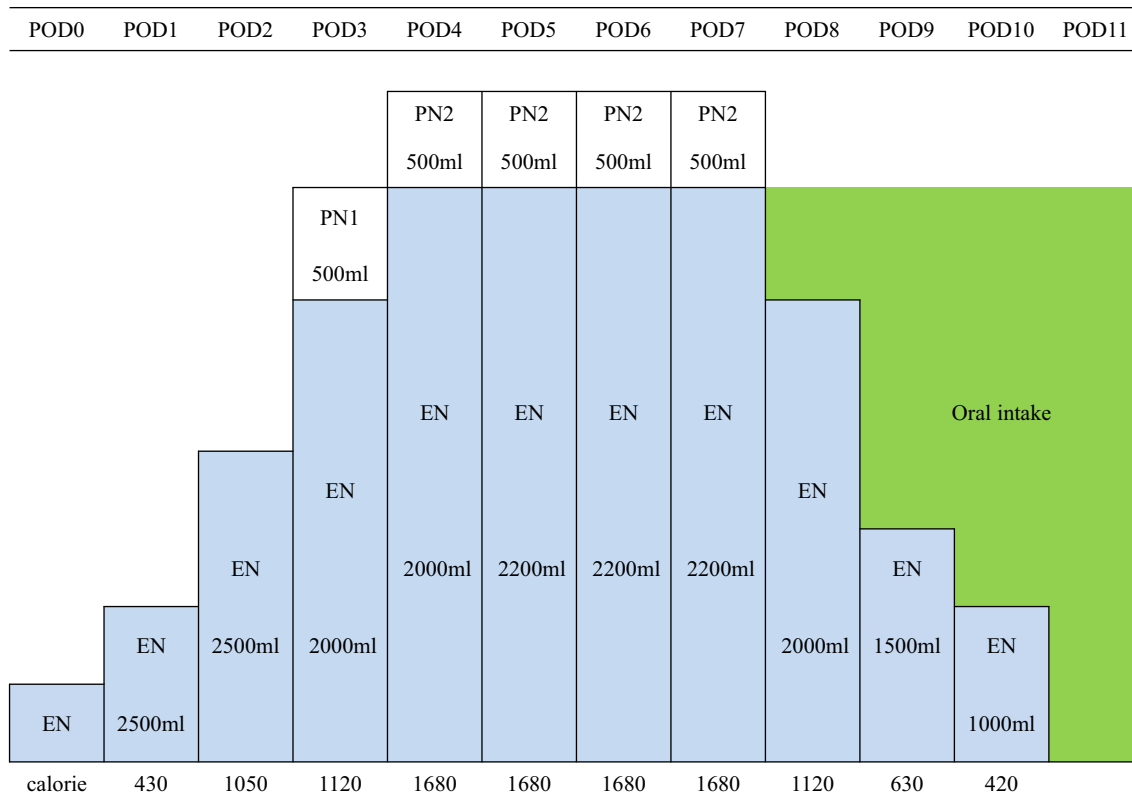
| POD0 | POD1 | POD2 | POD3 | POD4 | POD5 | POD6 | POD7 | POD8 | POD9 | POD10 | POD11 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | PN2 500ml | PN2 500ml | PN2 500ml | PN2 500ml | | | | |
| | | | PN1 500ml | EN | EN | EN | EN | | | Oral intake | |
| | | EN | EN | | | | | EN | | | |
| | EN | 2500ml | 2000ml | EN 2000ml | EN 2200ml | EN 2200ml | EN 2200ml | | EN | | |
| EN | 2500ml | | | | | | | EN 2000ml | 1500ml | EN 1000ml | |
| calorie | 430 | 1050 | 1120 | 1680 | 1680 | 1680 | 1680 | 1120 | 630 | 420 | |

**FIG. 2** Protocol for enteral nutrition. EN1: 1 kcal/1 mL, osmotic pressure 760 mOsm/L (free amino acid 44 g/L, carbohydrate 211 g/L, lipid 1.7 g/L). *POD* postoperative day

function.[19] Moreover, EN normalizes the immune system.[20] In this study, the incidence of pneumonia was less in the EN group. EN may also reduce infectious complications in patients after thoracoscopic esophagectomy. To clarify the effect of EN for postoperative complications, a greater number of patients need to be analyzed.

Unlike the previous study, no differences were observed in total bilirubin and CRP levels, and duration of ICU and postoperative hospital stay, in this study. For patients who underwent the thoracoscopic procedure and steroid therapy to reduce excessive inflammatory response and related complications, enteral feeding did not greatly contribute to their recovery.

Hyperglycemia is one of the most important complications of PN.[21] In our study, for the five patients with mild to moderate diabetes mellitus, the mean blood sugar levels until POD 14 were almost equivalent among the two groups. These results suggested that blood sugar could be controlled adequately by sliding-scale insulin therapy in both groups.

In seven patients, enteral feeding was needed after discharge. Four patients had dysphagia with recurrent laryngeal nerve paralysis, two experienced loss of appetite, and one had cerebral hemorrhage after esophagectomy. EN was particularly beneficial for patients with insufficient oral intake even after discharge.

## CONCLUSIONS

Postoperative EN was recommended after thoracoscopic esophagectomy to suppress both postoperative weight loss and the incidence of pneumonia. EN was also beneficial for patients with insufficient oral intake postsurgery.

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