Early Enteral Nutrition Versus Parenteral Nutrition After Resection of Esophageal Cancer: a Retrospective Analysis

Huan Ming Yu¹ · Cheng Wu Tang² · Wen Ming Feng² · Qiu Qiang Chen¹ · Yong Qiang Xu² · Ying Bao²

Received: 29 July 2015 / Accepted: 3 December 2015 / Published online: 16 December 2015
© Association of Surgeons of India 2015

Abstract This study aimed to compare the clinical outcomes and hospitalization cost between early enteral nutrition (EEN) and parenteral nutrition (PN) after resection of esophageal cancer. A total of 79 patients with esophageal cancer who underwent surgical treatment in our hospital from July 2010 to July 2013 were enrolled in this study. They were divided into EEN group ($n=39$) and PN group ($n=40$) based on the nutrition support modes. The clinical factors such as time to first fecal passage, postoperative albumin infusion, differences of serum albumin value, hospital stay, systematic inflammatory response syndrome (SIRS) duration, complications, initial hospitalization cost, and mortality were retrospectively compared. The EEN group had a significantly shorter hospital stay, lower initial hospitalization cost, earlier first fecal passage, and shorter duration of SIRS than PN group ($P<0.05$). The dose of albumin infusion was significantly smaller in EEN group ($P<0.05$) and the decreased value of serum albumin (Δalb) was more prominent in PN group compared with EEN group ($P<0.05$). The percentage of patients having any postoperative complication was much higher in PN group than EEN group ($P<0.05$), but there was no significant difference in in-hospital morbidity between two groups. Pneumonia was found significantly more frequent in PN group compared with EEN

group ($P<0.05$). Early EN started within 48 h after esophagectomy is safe, economic, and superior for reduction of postoperative complication, for promoting early recovery of intestinal movement, and for early recovery from systemic inflammation.

Keywords Esophageal cancer · Enteral nutrition · Complication · Parenteral nutrition

Introduction

Esophageal cancer is one of the common malignant tumors in the digestive tract, and China has the highest incidence and mortality rate of esophageal cancer all over the world [1]. Currently, surgery is still the best way for treatment of esophageal cancer [2], which is associated with significant risks of morbidity, with approximately one in three patients experiencing major complications, and an attendant in-hospital mortality rate of between 2 and 10 % [3, 4]. Esophagectomy for esophageal cancer is one of the most invasive procedures among gastrointestinal surgeries, and patients undergoing esophagectomy are unable to gain nutrition by mouth within the first few days after surgery. Thus, postoperative enteral nutrition (EN) and/or parenteral nutrition (PN) have become routine management in such cases, and recent studies demonstrated that EN initiated within 24–48 h after esophagectomy reduced the length of hospital stay [5, 6], postoperative morbidity, and the rate of life-threatening complications [7]. However, because some studies have not shown any clinical benefits with postoperative early enteral nutrition (EEN) after esophagectomy over PN [8, 9] and indicated the importance of PN after esophagectomy as a nutrition therapy [10], so the superiority of EEN after

✉ Cheng Wu Tang
tangche@sina.com

¹ Department of Thoracic Surgery, First People's Hospital Affiliated to Huzhou University Medical College, Huzhou, Zhejiang, China

² Department of General Surgery, First People's Hospital Affiliated to Huzhou University Medical College, Huzhou, Zhejiang, China

esophagectomy has remained controversial. The aim of the present retrospective study was to clarify the superiority of EEN for postoperative course compared with PN in patients with esophageal cancer.

Methodology

Patients

Between July 2010 and July 2013, 79 patients presenting to the Department of Thoracic Surgery at First People's Hospital Affiliated to Huzhou University Medical College with a clinical diagnosis of resectable esophageal cancer were enrolled of whom 39 patients received early enteral nutrition (EEN group), and 40 patients received parenteral nutrition (PN group) after esophagectomy. The exclusion criteria included the following: patients with metastatic disease; patients with a known immunologic disorder; emergency esophagectomy cases; patients with cardiac, liver, or renal failure; active small intestinal disease (e.g., Crohns disease); known allergy to any of the ingredients; poorly controlled diabetes; or existing use of fish oil/n-3 fatty acids supplements. Further exclusions established a priori were patients who had the nutrition support interrupted for greater than 3 days in the postoperative period. Patients whose thoracic duct was resected due to direct invasion of a tumor were also excluded because an acute obstruction of chyle flow can strongly affect the absorption of dietary fat, fluid homeostasis, or immune function.

Preoperative diagnoses were based on preoperative imaging studies, including contrast agent swallow studies, endoscopy, and conventional cross-sectional imaging studies (computed tomography). Histological evaluation of specimens obtained by preoperative endoscopically guided biopsy was performed in all cases. The patients' medical records were reviewed to determine the clinical disease stage, the surgical procedures performed, the histopathological diagnoses of the lesions, and the outcomes.

In all cases, esophagectomy—either transhiatal esophagectomy or transthoracic esophagectomy with 3-field lymph node dissection—was performed in the usual manner. In stage II and stage III disease, preoperative chemoradiotherapy or systemic chemotherapy was performed in principle and then followed by esophagectomy.

Nutritional Supports

EN group: The anesthetist and surgeon cooperated closely during the surgery. Under the guidance of the surgeon, jejunal feeding tube was nasally placed at 20–30 cm away

from distal Treitz ligament. On the first postoperative day (day 1), the patients were provided with routine peripheral intravenous infusion of glucose solution (2000–2500 mL) plus potassium chloride; furthermore, the 30 °C normal saline (250 mL) was instilled via the nasal-intestinal tube. At day 2, the patients were perfused with Peptisorb (NUTRICIA, Netherland) 500 mL at a constant speed (30–50 mL/h). The dose was gradually increased according to the patients' subjective feeling and tolerance. At day 3, the patients were tube-fed with Peptisorb 500 mL plus Nutrison Fibre (NUTRICIA, Netherland) 500 mL at a speed of 50–60 mL/h. At day 4, the patients were tube-fed with 1500–2000 mL of the products at a speed of 80–100 mL/h, reaching the full dose. The full dosage was provided in the following 4–6 days. The total amount of nutrient solution was calculated based on the total daily energy intake 125.52 kJ (30 kcal)/kg. During the perfusion, the tube was flushed every 4 h to maintain it unobstructed. Fluid warmer was applied to maintain the nutrient solution at a temperature of 38–42 °C. The initially insufficient fluid and heat were supplemented intravenously. PN group: PN was provided using a standard 3-l package containing compound amino acid, long-chain fat emulsion, glucose, vitamins, electrolytes, and trace elements via the central venous catheter after the surgery. Based on a total daily energy of 125.52 kJ (30 kcal)/kg, the carbohydrate:fat calorie percentage ratio was set at 2:1. At day 8, radiographic contrast agent swallow examination was performed in both group to evaluate the anastomosis and any passage problems. If this examination showed no leakage or obstruction, the nasogastric tube was removed, nutrition support was discontinued around day 8, and patients were provided with liquid diet at day 8, semi-liquid diet at day 10, and ordinary diet at day 12.

Outcome Measurements

Clinical factors such as age, sex, tumor stage according to the tumor-node-metastasis classification of the International Union Against cancer (6th edition) [11], bowel movement recovery expressed as days for first fecal passage, the dose of postoperative albumin infusion used, difference of serum albumin value between day 7 and pre-operation (Δ alb), duration of systematic inflammatory response syndrome (SIRS), incidence of postoperative complications, hospital stay, and initial hospitalization cost were retrospectively compared. All complications from surgery to discharge from hospital including major postoperative complications, specifically pneumonia, adult respiratory distress syndrome (ARDS), sepsis, enteritis, heart failure, respiratory failure, empyema, wound infection, renal failure, anastomotic leak, and in-hospital

mortality were retrospectively searched from patient records. Respiratory failure was defined as the requirement for mechanical ventilation beyond 24 h after surgery. ARDS and multiple organ failure were defined as per Bone et al. [12]. Sepsis required evidence of SIRS with microbiological evidence of infection, and the diagnosis of pneumonia required either positive sputum cultures or clear clinical and radiographic evidence of consolidation. SIRS was diagnosed by clinical manifestation of two or more of the following features: systolic blood pressure <90 mmHg, tachycardia >90/min, respiratory rate >20/min or peripheral arterial CO₂ tension (PaCO₂) <32 mmHg, temperature >38.0 °C or <36.0 °C, leukocytosis >12,000/μL or leukopenia <4000/μL, or 10% immature (band) forms.

Recurrent nerve palsy indicated as vocal cord function was assessed by laryngofiberscopy in all patients, regardless of the presence or absence of hoarseness, as previously described in [13]. Initial hospitalization cost referred to hospital billing for the admission for operation.

Statistical Analysis

All measurements were expressed as mean±SD. The statistical analyses were performed using the two-sample *t*

test and adjusted Chi-square test for the two groups. The Exact Chi-square test was also used if individual cell size was less than five counts. *P* value <0.05 was considered statistically significant.

Results

Patient Characteristics

Patient characteristics were well balanced. There were no statistically significant differences between the EEN and PN groups in patient characteristics, in terms of gender, age, site of lesion, preoperative nutritional conditions expressed by body mass index (BMI), body weight, or serum albumin values, preoperative adjuvant therapy, surgical approach, pathologic stage, and histological diagnosis (Table 1).

Clinical Outcomes

Clinical outcomes were shown in Table 2. The EEN group seemed to have had a shorter hospital stay and lower initial expense than the PN group (*P*<0.05). First fecal passage was observed significantly earlier in EEN group (*P*<0.05) and also the duration of SIRS was significantly

Table 1 Patient characteristics

		EEN (<i>n</i> =39)	PN (<i>n</i> =40)	<i>P</i> value
Gender	Male	29	30	0.9478
	Female	10	10	
Preoperative adjuvant therapy	Neoadjuvant	18	16	0.5730
	Chemoradiotherapy	9	11	
Site of lesion	Upper thoracic	9	11	0.5438
	Middle thoracic	18	21	
	Lower thoracic	12	8	
Pathologic stage	0	2	2	0.9418
	I	4	6	
	II	14	12	
	III	13	15	
	IV	6	5	
Histological diagnosis	Adenocarcinoma	9	6	0.6414
	Squamous cell carcinoma	27	30	
	Other	3	4	
Surgical approach	Transhiatal	25	30	0.2924
	Transthoracic	14	10	
Age (year)		64.6±8.1	66.8±9.4	0.2691
Operative time (min)		185.5±32.1	183.2±38.1	0.7727
Blood loss (ml)		351.2±50.3	365.7±43.2	0.1729
BMI (kg/m ²)		22.4±3.1	23.4±2.9	0.1427
Body weight (kg)		78.3±10.5	80.6±9.7	0.3149
Preoperative serum albumin (g/L)		33.1±8.3	34.2±9.5	0.5856

Table 2 Clinical outcomes

	EEN (<i>n</i> =39)	PN (<i>n</i> =40)	<i>P</i> value
First fecal passage (day)	2.8±1.1	3.7±1.4	0.0022
Hospital stay (day)	16.1±4.2	18.4±5.7	0.0450
Albumin infusion (g)	30.3±5.2	40.7±6.7	0.0000
Δalbumin (g/L)	−1.2±0.4	−2.4±0.7	0.0000
In-hospital mortality	0	1	1.0000
SIRS duration (day)	3.2±1.2	4.5±1.7	0.0002
Initial hospitalization cost (Chinese yuan)	25,873.7±1253.2	29,483.6±1432.7	0.0000

shorter in EEN group ($P<0.05$). The dose of albumin infusion was significantly smaller in EEN group ($P<0.05$), and the decreased value of serum albumin (Δalb) was more prominent in PN group compared with EEN group ($P<0.05$).

The percentage of patients having any postoperative complication was much higher in PN group than EEN group (19/40 vs. 10/39, $P<0.05$) (Table 3), but there was no significant difference in in-hospital morbidity between two groups (Table 2). Further analysis about postoperative complications was performed, and pneumonia was found significantly more frequent in PN group compared with EEN group ($P<0.05$) (Table 3).

Discussion

In general, esophageal cancer is a common malignant tumor of the gastrointestinal tract. Patients with esophageal cancer often already have poor nutritional status and low immune function due to several possible factors including esophageal stenosis, their habits, preoperative systemic chemotherapy, or the systemic effect of their neoplasm [14]. Esophagectomy is an exemplar of controlled major trauma, and is associated with profound perturbations in the metabolic, endocrine,

neuroendocrine, and immune system [15]. The surgical trauma, postoperative catabolism, and the further decreased immune function after surgery will result in a series of postoperative complication and poor recovery. Therefore, it is critically important to improve the postoperative nutritional status and restore the immune function in patients with esophageal cancer.

EN has been well recognized as an economical, safe, and effective nutritional support method that complies with the physiological state, helps to maintain the digestive tract morphology and function, operates in a simple way, and has few complications [16]. In addition to these advantages, enteral nutrition during and after certain surgical insults has other benefits including inhibition of energy expenditure [17], the cytokine response [18], the secretion of stress hormones [19], and bacterial translocation [20]. A landmark meta-analysis performed by Moore et al. [21] showed that the incidence of infectious and noninfectious complications in trauma patients managed with enteral nutrition was significantly lower than in patients managed with parenteral nutrition.

However, reports of the effects of postoperative early enteral nutrition (EEN) specifically in patients undergoing esophagectomy were limited [14, 22, 23]. Furthermore, most clinical studies did not compare enteral nutrition and total parenteral nutrition in a randomized fashion [14, 22, 24]. Of the studies performed in a prospective randomized fashion [9, 25, 26], the patients studied were not limited to esophageal cancer patients, such that the bona fide effects of EEN in esophageal surgery were not clear. Furthermore, the term “early” was defined as EN started within 24–48 h after admission or surgery [27]; however, EN started within 24 h had shown no advantage for the postoperative course in esophageal cancer [28].

Therefore, in the present study, we initiated EEN within 48 h after esophagectomy. We found that the patients of the EEN group showed a significantly shorter hospital stay, lower initial hospitalization cost, earlier first fecal passage, and shorter duration of SIRS than PN group.

The alleviated decrease of serum albumin and reduced dose of albumin infusion indicated that EEN was more efficient and economic for nutritional status improvement after

Table 3 Postoperative complications

	EEN (<i>n</i> =39)	PN (<i>n</i> =40)	<i>P</i> value
Postoperative complication (%)	10 (25.6 %)	19 (47.5 %)	0.0439
Anastomotic leakage	1	4	0.3708
Pneumonia	3	10	0.0381
Wound infection	5	10	0.1676
Renal failure	1	1	1.0000
Heart failure	1	2	0.9822
Sepsis	2	5	0.4706
Empyema	1	3	0.6261
ARDS	1	2	0.9822
Enteritis/intestinal ischemia	2	6	0.2968
Delayed gastric emptying	5	8	0.4177
Recurrent nerve palsy	8	9	0.8299

esophagectomy. Though there was no significant difference in in-hospital morbidity between two groups, less postoperative complication especially pneumonia was found in EEN group than in PN group.

The present study has several limitations. Because the length of the postoperative hospital stay can be influenced by a patient's social circumstances, the present study was possibly biased. Furthermore, the present study was still a retrospective study, preoperative nutritional assessment were determined by BMI, and body weight and albumin which were now considered as an acute phase reactant were the only available biochemistry data as a representative of patients nutritional status several years ago in our hospital.

In conclusion, Early EN started within 48 h after esophagectomy is well tolerable. It is safe, economic, and superior for reduction of postoperative complication, for promoting early recovery of intestinal movement, and for early recovery from systemic inflammation.

Authors' Contributions Huan Ming Yu and Cheng Wu Tang designed the study and wrote the manuscript, Qiu Qiang Chen, Yong Qiang Xu, and Ying Bao did the clinical and follow-up work, and Wen Ming Feng provided the collection of all the human material in addition to providing financial support for this work.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no competing interest.

Ethics Approval and Consent to Participate Written informed consent was obtained from all patients. Approval of the study was obtained from the Institutional Review Board.

References

- Wang JB, Fan JH, Liang H, Li J, Xiao HJ, Wei WQ, Dawsey SM, Qiao YL, Boffetta P (2012) Attributable causes of esophageal cancer incidence and mortality in China. *PLoS One* 7(8):e42281. doi:10.1371/journal.pone.0042281
- Biere SS, van Berge Henegouwen MI, Maas KW, Bonavina L, Rosman C, Garcia JR, Gisbertz SS, Klinkenbijn JH, Hollmann MW, de Lange ES, Bonjer HJ, van der Peet DL, Cuesta MA (2012) Minimally invasive versus open oesophagectomy for patients with oesophageal cancer: a multicentre, open-label, randomised controlled trial. *Lancet* 379(9829):1887–1892. doi:10.1016/S0140-6736(12)60516-9
- Bailey SH, Bull DA, Harpole DH, Rentz JJ, Neumayer LA, Pappas TN, Daley J, Henderson WG, Krasnicka B, Khuri SF (2003) Outcomes after esophagectomy: a ten-year prospective cohort. *Ann Thorac Surg* 75(1):217–222, discussion 222
- Enzinger PC, Mayer RJ (2003) Esophageal cancer. *N Engl J Med* 349(23):2241–2252. doi:10.1056/NEJMra035010
- Jiang K, Cheng L, Wang JJ, Li JS, Nie J (2009) Fast track clinical pathway implications in esophagogastrectomy. *World J Gastroenterol* 15(4):496–501
- Cao S, Zhao G, Cui J, Dong Q, Qi S, Xin Y, Shen B, Guo Q (2013) Fast-track rehabilitation program and conventional care after esophagectomy: a retrospective controlled cohort study. *Support Care Cancer* 21(3):707–714. doi:10.1007/s00520-012-1570-0
- Fujita T, Daiko H, Nishimura M (2012) Early enteral nutrition reduces the rate of life-threatening complications after thoracic esophagectomy in patients with esophageal cancer. *European surgical research Europäische chirurgische Forschung Recherches chirurgicales europeennes* 48(2):79–84. doi:10.1159/000336574
- Page RD, Oo AY, Russell GN, Pennefather SH (2002) Intravenous hydration versus naso-jejunal enteral feeding after esophagectomy: a randomised study. *Eur J Cardiothorac Surg* 22(5):666–672
- Watters JM, Kirkpatrick SM, Norris SB, Shanji FM, Wells GA (1997) Immediate postoperative enteral feeding results in impaired respiratory mechanics and decreased mobility. *Ann Surg* 226(3):369–377, discussion 377–380
- Llop-Talaveron JM, Farran-Teixidor L, Badia-Tahull MB, Virgili-Casas M, Leiva-Badosa E, Galan-Guzman MC, Miro-Martin M, Aranda-Danso H (2014) Artificial nutritional support in cancer patients after esophagectomy: 11 years of experience. *Nutr Cancer* 66(6):1038–1046. doi:10.1080/01635581.2014.939292
- Sobin LH, Wittekind C (2002) TNM Classification of Malignant Tumours, 6th edn. John Wiley & Sons, Hoboken, New York
- Smith T, Elia M (2006) Artificial nutrition support in hospital: indications and complications. *Clin Med* 6(5):457–460. doi:10.7861/clinmedicine.6-5-457
- Kosugi S, Kanda T, Yajima K, Ishikawa T, Hatakeyama K (2011) Risk factors that influence early death due to cancer recurrence after extended radical esophagectomy with three-field lymph node dissection. *Ann Surg Oncol* 18(10):2961–2967. doi:10.1245/s10434-011-1712-5
- Gabor S, Renner H, Matzi V, Ratzenhofer B, Lindenmann J, Sankin O, Pinter H, Maier A, Smolle J, Smolle-Juttner FM (2005) Early enteral feeding compared with parenteral nutrition after oesophageal or oesophagogastric resection and reconstruction. *Br J Nutr* 93(4):509–513
- Sweeney KJ, Kell MR, Ravi N, Reynolds JV (2005) Major upper gastrointestinal surgery is associated with an antigen-dependent proinflammatory T cell response. *Br J Surg* 92(8):989–995. doi:10.1002/bjs.4844
- Heyland DK, Cook DJ, Guyatt GH (1993) Enteral nutrition in the critically ill patient: a critical review of the evidence. *Intensive Care Med* 19(8):435–442
- Mochizuki H, Trocki O, Dominioni L, Brackett KA, Joffe SN, Alexander JW (1984) Mechanism of prevention of postburn hypermetabolism and catabolism by early enteral feeding. *Ann Surg* 200(3):297–310
- Fong YM, Marano MA, Barber A, He W, Moldawer LL, Bushman ED, Coyle SM, Shires GT, Lowry SF (1989) Total parenteral nutrition and bowel rest modify the metabolic response to endotoxin in humans. *Ann Surg* 210(4):449–456, discussion 456–447
- Saito H, Trocki O, Alexander JW, Kopcha R, Heyd T, Joffe SN (1987) The effect of route of nutrient administration on the nutritional state, catabolic hormone secretion, and gut mucosal integrity after burn injury. *JPEN J Parenter Enteral Nutr* 11(1):1–7
- Lin MT, Saito H, Fukushima R, Inaba T, Fukatsu K, Inoue T, Furukawa S, Han I, Muto T (1996) Route of nutritional supply influences local, systemic, and remote organ responses to intraperitoneal bacterial challenge. *Ann Surg* 223(1):84–93
- Moore FA, Feliciano DV, Andrassy RJ, McArdle AH, Booth FV, Morgenstein-Wagner TB, Kellum JM Jr, Welling RE, Moore EE (1992) Early enteral feeding, compared with parenteral, reduces postoperative septic complications. The results of a meta-analysis. *Ann Surg* 216(2):172–183
- Mercer CD, Mungara A (1996) Enteral feeding in esophageal surgery. *Nutrition* 12(3):200–201

23. Aiko S, Yoshizumi Y, Sugiura Y, Matsuyama T, Naito Y, Matsuzaki J, Maehara T (2001) Beneficial effects of immediate enteral nutrition after esophageal cancer surgery. *Surg Today* 31(11):971–978
24. Ryan AM, Rowley SP, Healy LA, Flood PM, Ravi N, Reynolds JV (2006) Post-oesophagectomy early enteral nutrition via a needle catheter jejunostomy: 8-year experience at a specialist unit. *Clin Nutr* 25(3):386–393. doi:[10.1016/j.clnu.2005.12.003](https://doi.org/10.1016/j.clnu.2005.12.003)
25. Baigrie RJ, Devitt PG, Watkin DS (1996) Enteral versus parenteral nutrition after oesophagogastric surgery: a prospective randomized comparison. *Aust N Z J Surg* 66(10):668–670
26. Heslin MJ, Latkany L, Leung D, Brooks AD, Hochwald SN, Pisters PW, Shike M, Brennan MF (1997) A prospective, randomized trial of early enteral feeding after resection of upper gastrointestinal malignancy. *Ann Surg* 226(4):567–577, discussion 577–580
27. Doig GS, Heighes PT, Simpson F, Sweetman EA, Davies AR (2009) Early enteral nutrition, provided within 24 h of injury or intensive care unit admission, significantly reduces mortality in critically ill patients: a meta-analysis of randomised controlled trials. *Intensive Care Med* 35(12):2018–2027. doi:[10.1007/s00134-009-1664-4](https://doi.org/10.1007/s00134-009-1664-4)
28. Manba N, Koyama Y, Kosugi S, Ishikawa T, Ichikawa H, Minagawa M, Kobayashi T, Wakai T (2014) Is early enteral nutrition initiated within 24 hours better for the postoperative course in esophageal cancer surgery? *J Clin Med Res* 6(1):53–58. doi:[10.4021/jocmr1665w](https://doi.org/10.4021/jocmr1665w)