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**ORIGINAL RESEARCH**

# Limited Efficacy of Early Enteral Nutrition in Patients after Total Gastrectomy

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## ABSTRACT

*Background*: Evaluable data documenting the efficacy of early enteral nutrition (EEN) in patients after total gastrectomy are still limited. *Aims*: This study aimed to evaluate the clinical efficacy of EEN through a nasojejunal tube on the recovery of patients after total gastrectomy compared with that of patients receiving only total parenteral nutrition (TPN). *Materials and Methods*: One hundred and sixteen patients who underwent total gastrectomy were divided into the EEN and TPN groups. The clinical recovery and postoperative complications of these two groups were compared. *Results*: There were 62 patients in the EEN group and 54 in the TPN group. The postoperative length of hospital stay, time of flatus passage, and time to start a semisolid diet were similar in the two groups. In the TPN group, however, patients started a liquid diet earlier. No difference in any postoperative complications or perioperative death were found between the EEN and TPN groups. *Conclusion*: Since there was no significant difference regarding either the postoperative recovery course or complications, the routine placement of a nasojejunal tube for EEN is unnecessary in elective total gastrectomy.

**Keywords:** nasojejunal tube; early enteral nutrition; gastric cancer; total gastrectomy; complication; leakage

## INTRODUCTION

Nutritional status is a major factor determining the outcome of surgery. Due to anorexia, dietary restrictions, malabsorption, and intestinal losses, patients who have undergone gastrointestinal surgery frequently suffer from malnutrition, which leads to increased postoperative morbidity and extended hospitalization [1–3]. Therefore, artificial nutrition is suggested when oral intake is likely to be absent for a period of 5–7 days. Total parenteral nutrition (TPN) support was initially used to reduce the impact of malnutrition, yet most of these trials turned out to be profitless or associated with increased infectious complications [4, 5]. It is evident that whenever safe and efficient access to a functional gastrointestinal tract is available, gut feeding is preferable to TPN [6], which has been proved by the benefits of enteral nutrition, including the prevention of mucosal atrophy, better substrate utilization, the preservation of normal gut flora, and immune competence [7–9]. It has been reported that early enteral nutrition (EEN) has decreased the risk of septic morbidity and infectious complications more effectively than TPN in burnt, septic, traumatic, or injured patients [6, 10–12].

However, the true biological and clinical benefits of EEN gained by gastric cancer patients after total gastrectomy is not yet clear. To our knowledge, methodological limitations existed in previous studies in this field. Where the time of administration of enteral nutrition (EN) or parenteral nutrition (PN) varied, nutrition was both preoperatively and postoperatively given, and the patient populations were heterogeneous in the primary disease [13, 14].

Previous studies have proved that neither nasogastric nor nasojejunal decompression are necessary after total gastrectomy. Since most of the patients after total gastrectomy require artificial enteral supplementation for only a short period, in this study, we provided EEN through a nasojejunal tube that was placed during operation. The objective of this study is to compare the efficacy of EEN on the recovery of and postoperative complications in gastric cancer patients after total gastrectomy with that of TPN.

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## MATERIALS AND METHODS

### Patient Population

We conducted a retrospective review of patients in whom total gastrectomy with Roux-en-Y esophagojejunostomy had been performed at the Department of General Surgery, Affiliated ZhongDa Hospital, Southeast University between November 2004 and March 2010. During this period, 344 patients with gastric cancer were admitted to our department, of whom three patients had residual gastric cancer, seven gave up treatment, 213 had partial gastrectomies, and three had bypass procedures. Two of the patients were excluded from this study because of insufficient medical data, and a total of 116 were finally enrolled.

Nasojejunal tube feeding has been used in our department since 2004, and the rate of patients using it has increased since then (from 1/3 EEN before 2007 to 2/3 after 2007). Therefore, the 116 patients were classified into two groups: an EEN group ($n = 62$) and a TPN group ($n = 54$). Written consent was obtained from all patients before operation, and the study protocol was approved by the ethical committee of our hospital. No formal inquiry was made to any pharmaceutical companies.



### Operation and Tube Feeding

General anesthesia and a standard midline laparotomy incision were applied to all patients. The continuity of the alimentary tract was restored with an end-to-side mechanical Roux-en-Y esophagojejunostomy (25 mm circular stapling device), while the extension of lymphadenectomy was at the surgeon's discretion. Patients in the EEN group underwent placement of a single-lumen nasojejunal tube (Pur tube, CH10/3.33 mm; Nutricia Medical Device BV), in which the tube was fed into the jejunum lumen and the catheter tip was then advanced 10–20 cm beyond the site of the jejunum–jejunum anastomosis.

In the EEN group, a stepwise increase of intake calories from enteral nutrition was scheduled and started within 24 hr of operation. On the first postoperative day, around 250 ml of 5% dextrose (20–30 ml/hr) was only infused, which was controlled by an enteral feeding pump. From the second postoperative day, enteral nutrients were given at a rate of about 25 ml/hr and increased by about 25 ml/hr each day until the target rate (maximum 100–120 ml/hr) was achieved, with a goal of 20–25 kcal/kg per day, as tolerated by the patient. The patient's ability to tolerate this tube feeding was recorded daily, noting symptoms such as cramping, distention, nausea, and diarrhea. Since it is impossible to provide enough nutrition at the very beginning postoperatively, patients receiving EEN were also supplied by PN for a short period of time, and the calories administered by PN were gradually reduced as those administered by EN were increased. PN was ceased when the number of calories administered by EN reached around 1,000 kcal/day or more. Oral diet was introduced gradually on day 6 or 7 postoperatively, as the patient desired. The calories from EN were then gradually decreased due to the increase in the calorie amount from the oral diet, and finally the tube was withdrawn. The TPN group was given conventional postoperative care until the maintenance of oral intake took place. TPN formulation contains amino acids, glucose and fat emulsion, plus electrolytes, trace elements, vitamins, and additives. Caloric distribution is 50–60% glucose and 40–50%fat.

The enteral nutrient used in this study was standard commercial enteral nutrition suspension (mainly: Fresubin [Fresenius Kabi Deutschland GmbH], or TPF or TP-MCT [NUTRICIA or other similar commercial products.], which provided 500 kcal/500 ml, including an adequate supply of fatty acid, protein, trace elements, and vitamins. During the postoperative period, patients were evaluated for a number of symptoms: nausea, vomiting, abdominal cramping, abdominal distention, and diarrhea. The dates of the postoperative days when the first passage of flatus was observed and when the first liquid and solid diets were ingested and tolerated were recorded.

The demographic data, preoperative risk factors, pathological variables, operative factors, and associated pathological conditions were recorded.

The complications were also retrieved retrospectively from the hospital records. Length of hospital stay was defined as the period from the day of operation to the day of discharge. The discharge criteria consisted of three conditions: (1) the patient had not had a high fever for over 2 days, nor any inflammatory signs; (2) the patient was able to eat more than half of a solid diet; and (3) the patient was able to treat his own operation wound without any assistance.

### Statistical Analysis

Quantitative variables, presented as mean (SD), were analyzed by Student's *t*-test. Qualitative variables, expressed as number (percentage), were analyzed using Fisher's exact test. All analyses were performed with SPSS 13.0 software. Differences were considered statistically significant at $P < .05$.

## RESULTS

A total of 116 patients participated in the study. All patients were aged between 38 and 82 years, and all underwent total gastrectomy and Roux-en-Y esophagojejunostomy. The baseline characteristics in terms of age, gender, body mass index (BMI), biochemical parameters of nutritional status, comorbidity, tumor site, operating time, and American Joint Committee on Cancer/Union Internationale Contre le Cancer TNM stage

TABLE 1 Baseline characteristic of the two groups

| Characteristic | TPN ($n = 54$) | EEN ($n = 62$) | $P$ value |
|---|---|---|---|
| Male/female ratio | 40:14 | 48:14 | .67 |
| Age, mean ± *sd*, years | 60.94 ± 11.26 | 61.27 ± 10.19 | .87 |
| Age over 70 years | 42(91.36%) | 49(70.30%) | .87 |
| BMI(kg/m$^2$, $\bar{x} \pm sd$) | 23.73 ± 1.60 | 22.37 ± 4.44 | .20 |
| Preoperative morbidity (*N*,%) | (18, 33.33%) | (18, 29.03%) | .62 |
| Preoperative HB (g/L, $\bar{x} \pm s$) | 114.16 ± 20.70 | 112.00 ± 30.42 | .65 |
| Preoperative ALB (g/L, $\bar{x} \pm s$) | 34.77 ± 5.42 | 29.70 ± 4.24 | .27 |
| Albumin used before operation (g, $\bar{x} \pm s$) | 32 ± 16.43 | 15 ± 12.91 | .14 |
| Tumor site | | | >.05 |
| Proximal third | 6 | 9 | |
| Middle third | 32 | 38 | |
| Lower third | 16 | 15 | |
| TNM stage | | | .52 |
| I | 8 | 4 | |
| II | 7 | 9 | |
| III | 21 | 28 | |
| IV | 18 | 21 | |
| ASA classification | | | .38 |
| I | 1 | 0 | |
| II | 50 | 57 | |
| III | 2 | 1 | |
| IV | 1 | 4 | |
| Radical/palliative resection ratio | 42:12 | 49:13 | .87 |
| Operating time | 247.14±58.95 | 242.28±43.11 | .63 |

BMI Body Mass Index; HB hemoglobin; ALB albumin.



(sixth edition) were comparable between the EEN and TPN groups (Table 1). Although EEN was well tolerated by most of the patients, two cases were allocated to the TPN group, since they pulled out their tubes by themselves at the very beginning of enteral feeding, and EEN was stopped at once.

The nasojejunal feeding tube was placed without difficulties in all patients. The goal of daily total caloric intake was 25–30 kcal/kg. In the EEN group, early enteral feeding calories increased daily, and leveled off over 4–5 days. The enteral feeding group made up approximately 60–70% of the total caloric intake, and EN was maintained for a period of time and then decreased slowly as oral feeding was introduced. The source of intravenous calories was mainly dextrose, fatty acid, and amino acid in the intravenous fluid. We did not routinely use motility agents, such as metoclopramide, postoperatively.

The postoperative courses of the patients in the two groups were similar, and the patients in both groups received a similar amount of albumin infusion. The serum albumin levels were also comparable on postoperative days 5–7. The postoperative length of hospital stay, time of flatus passage, and time to start a semisolid diet were also similar in the two groups. The only difference was that in the TPN group, patients started a liquid diet earlier (Table 2).

Table 3 shows the prevalence of minor complications (noninfectious complications) and major complications (surgical and infectious complications) in the two groups. In the EEN group, abdominal distension and diarrhea developed a bit more frequently during the postoperative period; however, the difference did not reach statistical significance between the two groups. The onset of symptoms occurred on the initiation of early postoperative enteral feeding, and could

TABLE 2 Postoperative courses of patients in the two groups

| Variable | TPN ($n = 54$) | EEN ($n = 62$) | $P$ value |
|---|---|---|---|
| Albumin infused postoperatively (g, $x \pm s$) | 40.00 ± 42.27 | 43.45 ± 36.10 | .80 |
| Serum albumin level 5–7 days postoperatively (g/L, $x \pm s$) | 30.42 ± 3.99 | 29.7 ± 4.24 | .29 |
| Time to passage of flatus (day, $x \pm s$) | 4.55 ± 1.62 | 4.84 ± 1.50 | .35 |
| Time to passage of stool (day, $x \pm s$) | 5.56 ± 1.45 | 6.08 ± 1.57 | .11 |
| Time to starting liquid diet (day, $x \pm s$) | 6.21 ± 1.74 | 7.63 ± 2.33 | .001 |
| Time to starting semisolid diet (day, $x \pm s$) | 10.29 ± 4.09 | 10.92 ± 5.98 | .61 |
| Postoperative length of hospital stay (day, $x \pm s$) | 15.41 ± 11.57 | 15.00 ± 7.31 | .39 |

TPN total parenteral nutrition; EEN early enteral nutrition.

TABLE 3 Postoperative complications in the two groups

| Postoperative complications | TPN ($n = 54$) | EEN ($n = 62$) | $P$ value |
|---|---|---|---|
| Major complications (surgical and infectious complications) | | | |
| *Pneumonia/pleural effusion* | 2 (3.70%) | 4 (6.45%) | .51 |
| *Wound infection* | 2 (3.70%) | 2 (3.70%) | .88 |
| *Abdominal infection/abscess* | 5 (1.85%) | 2 (3.23%) | .17 |
| *Intestinal obstruction* | 2 (3.70%) | 0 | .13 |
| *Anastomotic leak* | 0 | 1 (1.61%) | .28 |
| *Lymphoid leak* | 1 (1.85%) | 0 | .29 |
| *Duodenal stump leak* | 0 | 1 (1.61%) | .35 |
| *Anastomotic stenosis* | 0 | 1 (1.61%) | .35 |
| *Death* | 2 (3.70%) | 1 (1.61%) | .48 |
| Minor complications *(noninfectious complications)* | | | |
| *Nausea* | 2 (3.70%) | 3 (4.84%) | .76 |
| *Vomiting* | 2 (3.70%) | 2 (3.23%) | .88 |
| *Abdominal distention* | 1 (1.85%) | 3 (4.84%) | .38 |
| *Abdominal cramping* | 0 | 1 (1.61%) | .35 |
| *Diarrhea* | 1 (1.85%) | 3 (4.84%) | .38 |

TPN total parenteral nutrition; EEN early enteral nutrition.



be alleviated by slowing the infusion rate. Table 3 also lists the major complications and shows that there were no significant differences in the incidence of any major complications, including anastomotic leak, between the EEN and TPN groups. There were two cases of intestinal obstruction in the TPN group, one of which was cured with conservative treatment, while the other needed reoperation and was then cured. One patient with anastomotic leakage in the EEN group gave up treatment for financial reasons and died. There was no significant difference in overall postoperative mortality between the EEN and TPN groups (Table 3).

Analysis showed that patients aged over 70 years developed more major complications than younger patients (Table 4). We then examined two subgroups consisting of patients of different ages in both the EEN and TPN groups separately to find whether EEN had any beneficial effects on older patients. Tables 5 and 6 show that in both the younger and older subgroups, there was no considerable difference in the incidence of major complications between EEN- and TPN-treated patients.

## DISCUSSION

Upper gastrointestinal malignancies are known to have high rates of malnutrition, which occurs in about 60% of gastric cancer [15, 16] cases. Nutritional treatment is expected to decrease the possibility of postoperative complications. Previous recommendations demonstrated that TPN increased the overall risk of postoperative complications by 10% when it was administrated to nourished patients. Furthermore, hyperglycemia associated with TPN can lead to subsequent infectious complications [17–19]. The use of EEN following trauma, burns, or major intestinal surgery has gained favor in recent years. One reason lies in the fact that the gut plays an increasingly central role in maintaining nutritional status and regulating the immune system [20]. Investigators have suggested that the alterations of the natural gastrointestinal immunity and barrier function caused by extended bowel rest and TPN can be prevented by the use of EEN [21, 22].

Studies in the trauma and critical care literature have documented that the most severely injured or septic patients tend to benefit from an early enteral feeding regimen [11, 23], However, this result should not be generalized to elective surgical patients, and we suspect that EEN for elective surgical patients should be analyzed independently of that for critically ill patients, not only because critically ill patients generally face more risks but also because the underlying pathophysiology of critical illness is complex, variable, not well-defined, and different from that of surgical stress [24].

Although some meta-analyses of randomized controlled trial (RCT) studies comparing EN with PN in patients before or after surgery have suggested that EN

TABLE 4 Major complications in different age groups

| Age group | Complications | Non complications | $P$ value |
|---|---|---|---|
| Below 70 years ($n = 91$) | 8 | 83 | .001 |
| Over 70 years ($n = 25$) | 9 | 16 | |

TABLE 5 Major complications in the two groups in patients below 70 years

| Groups | Complications | Non complications | $P$ value |
|---|---|---|---|
| TPN ($n = 42$) | 3 | 39 | .61 |
| EEN ($n = 49$) | 5 | 44 | |

TPN total parenteral nutrition; EEN early enteral nutrition.

TABLE 6 Major complications in the two groups in patients over 70 years

| Groups | Complications | Non complications | *P* value |
|---|---|---|---|
| TPN ($n = 12$) | 5 | 7 | .57 |
| EEN ($n = 13$) | 4 | 9 | |

TPN total parenteral nutrition; EEN early enteral nutrition.

is better than conventional PN [25–28], a recent meta-analysis recommended that the use of EN is preferable to TPN after gastrointestinal surgery when possible and indicated [29]. However, these studies or reviews have several methodological limitations, such as the inclusion and exclusion criteria and varied time of administration of EN or PN. Furthermore, patients were not well distributed in the primary disease. Some studies have suggested that the use of EEN in patients after total gastrectomy was feasible, tolerated, and cheaper; however, only a small number of such patients were reported. Furthermore, firm conclusions in terms of the efficacy and complications of EEN after total gastrectomy were still scarce [30, 31]. Thus, whereas it was not clear whether EEN support to patients after total gastrectomy would be more beneficial than TPN support, this study allows a more precise estimation of the effect of EEN on this condition.

We chose the nasojejunal route for tube feeding since it proved to have good tube and intestinal tolerance in patients undergoing laparotomy for gastric pathology [30]. A previous study demonstrated that the routine placement of a nasojejunal tube for the purpose of decompression was unnecessary in elective total gastrectomy for gastric cancer [32, 33]. In the former study, however, a nasojejunal tube was not used for enteral feeding. In our present study, we provided EEN through the nasojejunal route to evaluate the hypothesis that the administration of EEN on patients after total gastrectomy was more beneficial than TPN.

In our study, we observed an overall abdominal discomfort rate of 20% in the EEN group, which was consistent with previous trials reporting that 24–50% of the gastric patients after EEN had abdominal symptoms [12, 34]. We also observed similar rates of discomfort between the EEN and TPN groups, which was reasonable since TPN was also associated with abdominal symptoms and increased diarrhea [30].

It was reported that EEN led to earlier passage of the first stool postoperatively although the first audible bowel sound after surgery did not differ [35]. However, we did not find any difference in the first passage of flatus or stool. This was reasonable, since in the present study all patients received commercial enteral nutrient with a lesser or no amount of fibers.

There was no difference in serum albumin levels in either the EEN or TPN group, which was not a surprise. Since serum albumin has a long half-life of 20 days, and its status for the assessment of nutritional support is controversial, the early postoperative period (7 days) may be too short to demonstrate changes in its level after supplementation.

According to our observations, there was no significant difference in either minor or major postoperative complications in the EEN and TPN groups after total gastrectomy, including lung infection, abdominal infection/abscess, and anastomotic leak, as well as death (Table 3). Although, in general, older patients (over 70 years old) experienced more complications in our present study, EEN also did not show any efficacy in these patients. Thus, our results show that postoperative EEN did not decrease morbidity or mortality more effectively than TPN in elective total gastrectomy. This observation can potentially be explained by several factors. First, patients in the current study were not severely malnourished by biochemical and nutritional indices. Second, elective surgical stress had different mechanisms from those of trauma or critically ill patients. Third, both TPN and EEN were able to provide sufficient nutritional support to these kinds of patients. Last, most of the patients began the consumption of oral intake on/around the postoperative seventh day.

In the present study, although we did not detect any difference in lung infection and pneumonia between the EEN and TPN groups, respiratory infection was still a large concern in patients with feeding tube placement [36].

In conclusion, EEN shows no beneficial effects on decreasing the risk of either minor or major complications. In addition, if a leak develops, placement of a nasojejunal tube is possible for all patients. Thus, we believe that EEN is not warranted in patients after total gastrectomy.

*Declaration of Interest*: The authors report no conflict of interest. The authors alone are responsible for the content and writing of this paper.

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