

Effect of preoperative nutrition therapy type and duration on short-time outcomes in gastric cancer patient with gastric outlet obstruction

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Abstract

Objective: To avoid perioperative complications caused malnutrition, nutrition therapy is necessary in gastric outlet obstruction (GOO) patients. Compared to parenteral nutrition (PN), enteral nutrition (EN) is associated with many advantages. This study aimed to investigate whether preoperative EN has beneficial clinical effects compared to preoperative PN in gastric cancer patients with GOO undergoing surgery.

Methods: According to the methods of preoperative nutrition therapy, 143 patients were divided into EN group (n=42) and PN group (n=101) between January 2013 and December 2017 at the Chinese People's Liberation Army General Hospital. Multiple logistic regression models were used to assess the association between the methods of preoperative nutrition therapy and postoperative day of flatus passage. The generalized additive model and two-piecewise linear regression model were used to calculate the inflection point of the preoperative nutritional therapy time on the postoperative day of flatus passage in the PN group.

Results: EN shortened the postoperative day of flatus passage in gastric cancer patients with GOO, which is a protective factor, especially in patients who underwent non-radical operations and the postoperative day of flatus passage reduced when the preoperative PN therapy was up to 3 d and a longer PN therapy (>3 d) did not accelerate the postoperative recovery of gastrointestinal functions.

Conclusions: Preoperative EN therapy would benefit gastric cancer patients with GOO by accelerating postoperative recovery. For patients with absolute obstruction, no more than 3-day PN therapy is recommended if patients can tolerate general anesthesia and surgery.

Keywords: Nutrition therapy; gastric cancer; gastric outlet obstruction; enteral nutrition; parenteral nutrition

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Introduction

Gastric outlet obstruction (GOO), a mechanical gastric emptying dysfunction, is mainly caused by cancer invasion or scarring after ulcer healing in the distal stomach (1). The main clinical symptoms are abdominal distension and

vomiting, which become increasingly severe as the disease progresses and ultimately result in dystrophy, general fatigue, water and electrolyte balance disorders (2,3). Surgical removal of the obstruction is the primary goal of treatment in GOO patients (4). However, edema of the stomach and malnutrition lower the function of immune

system, which increases the risk of perioperative complications (2). To avoid complications such as infection, anastomotic leakage, and preoperative decompression of the stomach, nutrition therapy is necessary in these patients (5).

Until recently, parenteral nutrition (PN) was preferred for ileus, dysmotility, and subacute obstruction (considered as intestinal failure) to maintain nutritional support until the underlying disease was corrected (6). However, PN, although effective in delivering nutrients, has serious metabolic complications and catheter-related bloodstream infections (7). Compared to PN, enteral nutrition (EN) is associated with improvements in gastrointestinal mucosal integrity, immune function, tissue repair responses, and less infectious complications. This translated into decreased nosocomial infections, multiorgan failure, mortality, hospital stay, and health-care costs (8-10).

Developments in techniques of enteral access enabled the application of EN over the past decade. Compared with PN, whether EN has protective or deleterious effects on gastric cancer patients with GOO remains controversial. Thus, we aimed to investigate whether preoperative EN had beneficial clinical effects compared with preoperative PN in short-time outcomes in GOO patients received surgical treatment.

Materials and methods

Research objects

Between January 2013 and December 2017, 157 patients were diagnosed as having gastric cancer with GOO at the Chinese People's Liberation Army General Hospital. The inclusion criteria are summarized as: 1) had no serious conditions due to which they could not tolerate general anesthesia and surgery; 2) were confirmed to have GOO with upper gastrointestinal contrast computed tomography (CT) or gastroscopy; and 3) had undergone surgery for obstruction. Patients were excluded if they received preoperative radiation or chemotherapy. Fourteen patients were excluded from the study because their clinical data were severely incomplete, which finally left 143 gastric cancer patients with GOO who were included in this study. According to the methods of preoperative nutrition therapy, the 143 patients were divided into enteral nutrition group (n=42, EN group) and parenteral nutrition group (n=101, PN group). Ethical approval for the retrospective study was obtained from the Ethical Committee of the Chinese PLA General Hospital.

Treatment and clinical criteria

The total daily energy requirement for each patient was at least 35 kcal/kg. In the EN group, the EN solution (Nutrison, 400 g/tin, Abbott Laboratories, Netherlands, United States) was fed through a nasojejunal feeding tube placed under a gastroscope or an X-ray before surgery. The total energy required in the PN group was attained by infusing the total PN. Additional water, electrolytes, intravenous vitamins, and trace elements were administered as needed. The nutritional risk screening (NRS) was assessed according to the NRS-2002 of the European Society of Parenteral Enteral Nutrition (11). The nutritional statuses were expressed by hemachrome (HB), total protein (TP), and albumin (ALB) levels. The surgical methods included distal gastrectomy, radical total gastrectomy, gastrojejunostomy, and jejunostomy. The reconstruction methods included Billroth I, Billroth II, and Roux-en-Y. The primary outcome was the postoperative day of flatus passage, and secondary outcomes were the postoperative day of drainage and postoperative hospital stay. Postoperative complications including duodenal stump fistula, anastomotic leakage or stenosis, gastric retention, intestinal paralysis, postoperative hemorrhage, pancreatic leakage, pleural or peritoneal effusion, pyothorax, pyocelia, upper respiratory infection, central venous catheter-associated infection, hypoalbuminemia, arrhythmia, bacteremia, fungal infection, hypokalemia or hyperkalemia, phlebitis and skin rash were also recorded.

Statistical analysis

Continuous variables were expressed as $\bar{x} \pm s$, and normality of the distribution was checked using the Mann-Whitney U test and compared using an analysis of variance (Student's *t*-test or Mann-Whitney U test). Binomial and categorical data were evaluated using a Pearson's χ^2 or a two-tailed Fisher's exact test. Non-adjusted and adjusted multiple logistic regression models were used to assess the association between the methods of preoperative nutrition therapy and postoperative day of flatus passage. Covariates were considered in the adjusted model if the matched odds ratio changed by at least 10% as a result of adding those covariates (12). Next, non-linear relationship analyses were performed by a generalized additive model to determine the correlation between preoperative nutritional therapy time and postoperative day of flatus passage in the two groups. We further applied a two-piecewise linear regression model to calculate the inflection point of the preoperative nutritional therapy time on the postoperative

day of flatus passage in the PN group. All analyses were performed using the statistical software package R (<http://www.R-project.org>; The R Foundation for Statistical Computing, Vienna, Austria) and Empower States (<http://www.empowerstates.com>; X & Y Solutions, Inc., Boston, MA, USA). The 95% confidence interval (95% CI) was calculated for intergroup differences, and P values less than 0.05 (two-sided) were considered statistically significant.

Results

No thirty-day mortality occurred in either group. Demographic and clinical characteristics and surgical factors are summarized in *Table 1*. There was no significant difference in age, sex, body mass index (BMI), NRS score and diabetes between the two groups. The duration of inability to eat solid food was significantly longer in PN group than in EN group (10.0 d vs. 5.5 d, $P<0.001$). The preoperative nutritional therapy time was longer in PN group than in EN group (6.73 d vs. 5.95 d, $P=0.031$).

The tumor size and location, lymph node metastasis (N stage), distant metastasis (M stage), preoperative and postoperative HB, TP, and ALB of the two groups were not significantly different. Patients in PN group had more tumors of ulcerative type (47.78% vs. 21.95%, $P=0.031$) and moderate differentiation (29.17% vs. 7.14%, $P=0.022$) than those in EN group; however, patients in EN group

had more tumors of T4a stage (90.48% vs. 53.76%, $P<0.001$) than those in PN group (*Table 2*). The surgical treatments were similar in the two groups, including the percentage of radical and minimally invasive operations, surgical methods, reconstruction methods, estimated blood loss, and intraoperative transfusion of red blood cell or plasma.

Postoperative outcomes

The EN group had significantly shorter first flatus time than the PN group (3.79 d vs. 4.74 d, $P<0.001$); however, the pull nasogastric tube and drainage time were similar in the two groups. Postoperative complications were not significantly different between the two groups. The postoperative treatment time and hospital stay of EN group were shorter than those of PN group; however, the differences were not statistically significant. The difference in the total hospitalization costs between the two groups was not statistically significant (*Table 2*).

Effect of preoperative PN and EN on postoperative day of flatus passage

The univariable analyses showed that the method of preoperative nutrition therapy (EN or PN), diabetes, duration of inability to eat solid food, and percentage of radical operation were correlated with the postoperative

Table 1 Preoperative characteristics of patients in PN group and EN group

Characteristics	PN group (N=101) [n (%)]	EN group (N=42) [n (%)]	P
Age ($\bar{x}\pm s$) (year)	61.12 \pm 13.66	57.74 \pm 15.31	0.195
Sex			0.460
Male	69 (68.32)	26 (61.91)	
Female	32 (31.68)	16 (38.10)	
BMI ($\bar{x}\pm s$) (kg/m ²)	22.27 \pm 3.05	21.78 \pm 2.85	0.365
Diabetes			0.443
No	89 (88.12)	35 (83.33)	
Yes	12 (11.88)	7 (16.67)	
NRS score			0.499
3	60 (59.41)	29 (69.05)	
4	34 (33.66)	12 (28.57)	
5	7 (6.93)	1 (2.38)	
No solid food [Median (range)] (d)	10.0 (0, 120)	5.5 (0, 60)	<0.001
Preoperative nutritional therapy ($\bar{x}\pm s$) (d)	6.73 \pm 3.93	5.95 \pm 4.16	0.031

BMI, body mass index; NRS, nutritional risk screening. Continuous variables: Student's *t* test or Mann-Whitney U test; Binomial and categorical variables: Pearson's χ^2 or Fisher's exact test.

Table 2 Clinicopathological characteristics, treatment information and postoperative outcomes

Variables	PN group (N=101) [n (%)]	EN group (N=42) [n (%)]	P
Tumor size (cm) ($\bar{x}\pm s$)	5.71 \pm 2.48	5.98 \pm 1.99	0.544
Tumor location			0.516
Distal	84 (83.17)	33 (78.57)	
Middle	17 (16.83)	9 (21.43)	
Borrmann type			0.031
Mass	6 (6.67)	2 (4.88)	
Ulcerative	43 (47.78)	9 (21.95)	
Infiltrative ulcerative	17 (18.89)	12 (29.27)	
Diffuse infiltrative	24 (26.67)	18 (43.90)	
Degree of histologic differentiation			0.022
Well	1 (1.04)	2 (4.76)	
Moderately	28 (29.17)	3 (7.14)	
Poorly	56 (58.33)	32 (76.19)	
S-R cell or undifferentiated	11 (11.46)	5 (11.91)	
T			<0.001
T1	2 (2.15)	0 (0)	
T2	6 (6.45)	0 (0)	
T3	25 (26.88)	1 (2.38)	
T4a	50 (53.76)	38 (90.48)	
T4b	10 (10.75)	3 (7.14)	
N			0.082
N0	9 (10.71)	9 (22.50)	
N1	14 (16.67)	6 (15.00)	
N2	19 (22.62)	3 (7.50)	
N3a	35 (41.67)	21 (52.50)	
N3b	7 (8.33)	1 (2.50)	
M			0.151
M0	81 (86.17)	32 (76.19)	
M1	13 (13.83)	10 (23.81)	
Metastases			0.253
None	88 (87.13)	32 (76.19)	
Liver	5 (4.95)	3 (7.14)	
Peritoneal implantation	8 (7.92)	7 (16.67)	
Radical operation			0.357
No	26 (25.74)	14 (33.33)	
Yes	75 (74.26)	28 (66.67)	
MIS			0.036
No	53 (52.48)	30 (71.43)	
Yes	48 (47.53)	12 (28.57)	
Surgical methods			0.339
Distal gastrectomy	61 (60.40)	22 (52.38)	

Table 2 (continued)

Table 2 (continued)

Variables	PN group (N=101) [n (%)]	EN group (N=42) [n (%)]	P
Radical total gastrectomy	22 (21.78)	11 (26.19)	
Gastrojejunostomy	15 (14.85)	5 (11.91)	
Jejunostomy	3 (2.97)	4 (9.52)	
Reconstruction			0.636
Billroth I	15 (19.74)	5 (13.51)	
Billroth II	33 (43.42)	19 (51.35)	
Roux-en-Y	28 (36.84)	13 (35.14)	
Estimated blood loss (mL) [median (range)]	100 (10, 1,600)	125 (10, 1,200)	0.608
Transfusion (RBC, U) [median (range)]			0.286
No	0	0	
Yes	3 (1, 12)	2 (2, 6)	
Transfusion (plasma, U) [median (range)]			0.421
No	0	0	
Yes	2.4 (1.0, 6.5)	2.5 (1.1, 4.2)	
Complication			0.337
No	64 (63.37)	23 (54.76)	
Yes	37 (36.63)	19 (45.24)	
Postoperative PN (d) ($\bar{x}\pm s$)	5.89 \pm 3.08	5.49 \pm 1.54	0.430
Flatus (POD) ($\bar{x}\pm s$)	4.74 \pm 1.55	3.79 \pm 1.24	<0.001
Nasogastric tube (POD) ($\bar{x}\pm s$)	6.24 \pm 1.83	6.06 \pm 1.39	0.726
Drainage (POD) ($\bar{x}\pm s$)	9.46 \pm 4.97	8.14 \pm 2.93	0.111
Postoperative hospital stay (d) ($\bar{x}\pm s$)	14.27 \pm 11.53	12.64 \pm 4.52	0.378
Preoperative HB (g/L) ($\bar{x}\pm s$)	117.59 \pm 21.08	117.73 \pm 23.06	0.974
Postoperative HB (g/L) ($\bar{x}\pm s$)	116.62 \pm 15.80	115.03 \pm 17.83	0.614
Preoperative TP (g/L) ($\bar{x}\pm s$)	61.26 \pm 6.79	62.25 \pm 5.12	0.430
Postoperative TP (g/L) ($\bar{x}\pm s$)	54.91 \pm 7.06	54.76 \pm 5.72	0.903
Preoperative ALB (g/L) ($\bar{x}\pm s$)	35.72 \pm 4.69	34.76 \pm 4.42	0.263
Postoperative ALB (g/L) ($\bar{x}\pm s$)	31.88 \pm 4.30	32.16 \pm 3.60	0.709
Financial costs (CNY) ($\bar{x}\pm s$)	115,183.78 \pm 96,651.50	94,899.73 \pm 36,441.61	0.201

S-R cell, signet-ring cell; MIS, minimally invasive surgery; RBC, red blood cell; POD, postoperative day; HB, hemachrome; TP, total protein; ALB, albumin; PN, parenteral nutrition; EN, enteral nutrition. Continuous variables: Student's *t* test or Mann-Whitney U test; Binomial and categorical variables: Pearson's χ^2 or Fisher's exact tests.

day of flatus passage ($P<0.05$) (Table 3). The relationship between the preoperative PN or EN and postoperative day of passage in the different models is presented in Table 4. In the crude model, EN showed a negative correlation with the postoperative day of flatus passage ($\beta=-0.96$, 95% CI: -1.49 to -0.43, $P<0.001$). In the minimally adjusted model (adjusted preoperative nutritional therapy time, diabetes, and T stage), the result did not have any obvious changes ($\beta=-0.65$, 95% CI: -1.18 to -0.11, $P=0.020$). However, when we fully adjusted the model using preoperative

nutritional therapy time, diabetes, Borrmann type, degree of histologic differentiation, T stage, N stage, complication, and radical operation, we did not detect the correlation ($\beta=-0.30$, 95% CI: -0.83 to 0.22, $P=0.256$).

Effect of preoperative nutritional therapy time on postoperative day of flatus passage in PN group

As the preoperative nutritional therapy time was a continuous variable, an analysis of the non-linear

Table 3 Univariate analysis for postoperative day of flatus passage

Variables	β (95% CI)	P
Group		<0.001
PN	0	
EN	-0.96 (-1.49, -0.43)	
Age (year)	0.02 (0, 0.03)	0.077
Sex		0.922
Male	0	
Female	0.03 (-0.51, 0.56)	
BMI (kg/m ²)	-0.04 (-0.13, 0.04)	0.314
Diabetes		<0.001
No	0	
Yes	-1.26 (-1.97, -0.55)	
No solid food (d)	0.02 (0, 0.04)	0.017
NRS score		
3	0	
4	0.02 (-0.53, 0.57)	0.948
5	0.31 (-0.80, 1.42)	0.584
Preoperative nutritional therapy (d)	-0.03 (-0.09, 0.03)	0.351
Tumor size (cm)	-0.02 (-0.12, 0.09)	0.742
Tumor location		0.258
Distal	0	
Middle	-0.38 (-1.03, 0.27)	
Borrmann type		
Mass	0	
Ulcerative	0.70 (-0.28, 1.68)	0.162
Infiltrative ulcerative	-0.69 (-1.72, 0.34)	0.194
Diffuse infiltrative	-0.38 (-1.37, 0.62)	0.461
Degree of histologic differentiation		
Well	0	
Moderately	1.46 (-0.31, 3.23)	0.107
Poorly	0.72 (-0.99, 2.44)	0.413
S-R cell or undifferentiated	0.27 (-1.57, 2.11)	0.773
T		
T1	0	
T2	-1.00 (-3.30, 1.30)	0.395
T3	-0.69 (-2.76, 1.37)	0.512
T4a	-1.84 (-3.85, 0.17)	0.075
T4b	-1.31 (-3.45, 0.83)	0.233
N		
N0	0	
N1	0.03 (-0.88, 0.93)	0.952

Table 3 (continued)

Table 3 (continued)

Variables	β (95% CI)	P
N2	0.69 (-0.20, 1.57)	0.131
N3a	0.06 (-0.69, 0.82)	0.869
N3b	1.40 (0.22, 2.59)	0.022
M		0.064
M0	0	
M1	-0.64 (-1.30, 0.03)	
Metastases		
None	0	
Liver	-0.31 (-1.40, 0.78)	0.579
Peritoneal implantation	-0.76 (-1.57, 0.06)	0.071
Radical operation		0.017
No	0	
Yes	0.68 (0.13, 1.22)	
MIS		0.359
No	0	
Yes	0.24 (-0.27, 0.75)	
Reconstruction		
Billroth I	0	
Billroth II	-0.46 (-1.20, 0.28)	0.226
Roux-en-Y	-0.85 (-1.62, -0.08)	0.032
Estimated blood loss (mL)	0	0.127
Preoperative HB (g/L)	-0.01 (-0.02, 0.01)	0.407
Preoperative TP (g/L)	-0.04 (-0.08, 0.01)	0.100
Preoperative ALB (g/L)	-0.03 (-0.08, 0.03)	0.310

PN, parenteral nutrition; EN, enteral nutrition; BMI, body mass index; NRS, nutritional risk screening; HB, hemachrome; TP, total protein; ALB, albumin; β , effect size; 95% CI, 95% confidence interval.

Table 4 Relationship between preoperative PN or EN and postoperative day of flatus passage in different models

Group	Crude model		Minimally adjusted model		Fully adjusted model	
	β (95% CI)	P	β (95% CI)	P	β (95% CI)	P
EN	-0.96 (-1.49, -0.43)	<0.001	-0.65 (-1.18, -0.11)	0.020	-0.30 (-0.83, 0.22)	0.256

PN, parenteral nutrition; EN, enteral nutrition; β , effect size; 95% CI, 95% confidence interval. Minimally adjusted model adjusts for preoperative nutritional therapy time, diabetes and T; Fully adjusted model adjusts for preoperative nutritional therapy time, diabetes, Borrmann type, degree of histologic differentiation, T, N, complication and radical operation.

relationship could be conducted. As shown in *Figure 1A*, a threshold non-linear association between the preoperative nutritional therapy time and postoperative day of flatus passage was found by a generalized additive model in PN group ($P=0.022$), but not in EN group ($P=0.545$). Additionally, by the two-piecewise linear regression model, we calculated that the inflection point was 3 in PN group. On the left of the inflection point, the effect size (β), 95% CI and P value were -1.61, -3.10 to -0.11, and 0.038, respectively.

However, we observed no relationship between the preoperative nutritional therapy time and postoperative day of flatus passage to the right of the inflection point (-0.02, -0.09 to 0.06, $P=0.689$) (*Table 5, Figure 1B*). This indicated that the postoperative day of flatus passage reduced when the preoperative PN therapy was up to 3 d and that a longer PN therapy (>3 d) did not accelerate the postoperative recovery of gastrointestinal functions.

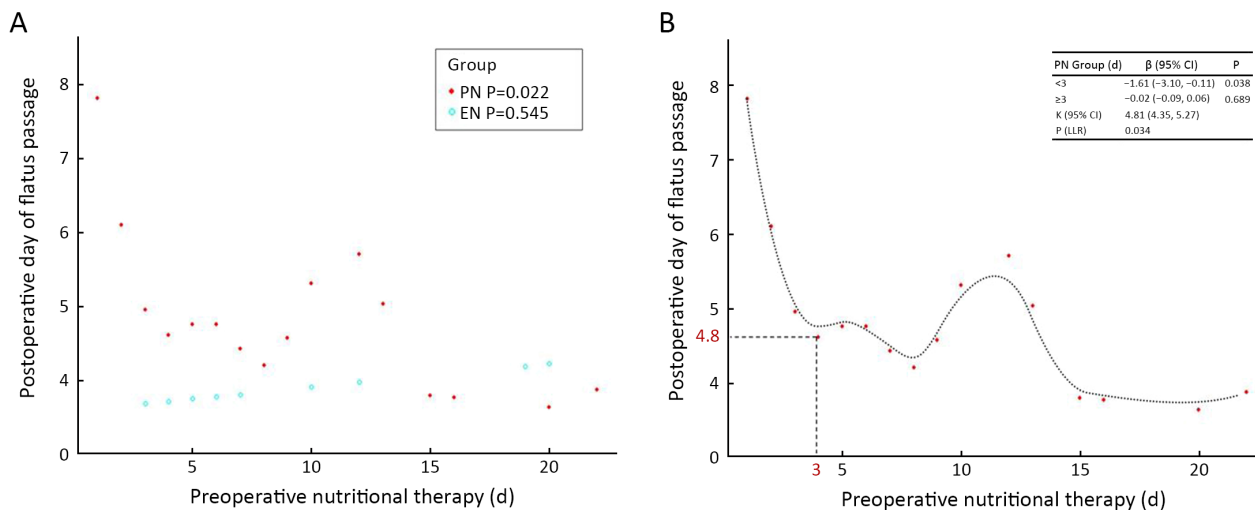


Figure 1 Effect of preoperative nutritional therapy time on postoperative day of flatus passage in PN group. (A) A threshold, non-linear association between the preoperative nutritional therapy time and postoperative day of flatus passage found by a generalized additive model in PN group (P=0.022) but not in EN group (P=0.545); (B) Two-piecewise linear regression model showing that the inflection point was 3 in PN group. When patients received preoperative PN treatment for 3 d, the postoperative day of flatus passage reached a relatively low value, 4.8 d. PN, parenteral nutrition; EN, enteral nutrition; β , effect size; 95% CI, 95% confidence interval.

Table 5 Results of two-piecewise linear regression model

Variables	PN		EN		Total	
	β (95% CI)	P	β (95% CI)	P	β (95% CI)	P
K point	3		12		3	
<K	-1.61 (-3.10, -0.11)	0.038	0 (-0.24, 0.24)	0.988	-1.26 (-2.29, -0.24)	0.017
$\geq K$	-0.02 (-0.09, 0.06)	0.689	0.21 (-0.11, 0.53)	0.201	0 (-0.06, 0.07)	0.921
K (95% CI)	4.81 (4.35, 5.27)		5.05 (3.50, 6.60)		4.39 (4.05, 4.73)	
P (LLR)	0.034		0.394		0.014	

K, inflection point of preoperative nutritional therapy time (d); LLR, log-likelihood ratio; PN, parenteral nutrition; EN, enteral nutrition; β , effect size; 95% CI, 95% confidence interval; Effect, postoperative day of flatus passage; Cause, preoperative nutritional therapy time; Adjusted for diabetes and T.

Subgroup analysis

As shown in Table 6, the test for interactions was significant for radical operations (P for interaction was 0.026). The odds ratio of preoperative nutritional therapy type on the postoperative day of flatus passage was larger in patients who did not undergo radical operation (-1.06, -2.02 to -0.10, P=0.037) than in those who underwent radical operation (-0.84, -1.47 to -0.22, P=0.010). This indicated that EN was a more effective protect factor for non-radical operations. The test for interactions was not statistically significant for other factors (Supplementary Table S1,S2).

Discussion

This study suggests that: 1) EN shortened the

postoperative day of flatus passage in gastric cancer patients with GOO, which is a protective factor, especially in patients who underwent non-radical operations and 2) the postoperative day of flatus passage reduced when the preoperative PN therapy was up to 3 d and a longer PN therapy (>3 d) did not accelerate the postoperative recovery of gastrointestinal functions.

Persistent vomiting, resulting in an excessive loss of digestive juices and difficulty absorbing nutrients, can lead to dehydration and electrolyte imbalance in the body. Previous reports have shown that the direct cause of death in >20% of patients with tumors is malnutrition (13). Surgery is an important intervention for the treatment of gastric cancer with GOO, with symptom remission rates as high as 72% (14). For patients undergoing surgery,

Table 6 Interaction of different preoperative nutritional therapy type (PN vs. EN) on postoperative day of flatus passage in prespecified and exploratory subgroups in each subgroup

Radical operation	N	Flatus (POD) [β (95% CI)]	P	P interaction
No	40	-1.06 (-2.02, -0.10)	0.037	0.026
Yes	103	-0.84 (-1.47, -0.22)	0.010	

PN, parenteral nutrition; EN, enteral nutrition; POD, postoperative day; β , effect size; 95% CI, 95% confidence interval.

preoperative malnutrition not only weakens muscle activity and the immune system, delays healing of incisions (15), and directly affects postoperative recovery and prognosis but also delays the best opportunity for gastric cancer patients with GOO to receive postoperative chemotherapy (16,17).

Therefore, most GOO patients need peri-operation nutrition therapy. PN has been an indispensable nutrition treatment for these patients, but lack of enteral feeding significantly increases infectious complications (18). EN can support patients with a variety of amino acid digestion and absorption problems, improve protein utilization to accelerate wound healing, activate the gastrointestinal nerve endocrine system, promote intestinal peristalsis, accelerate nutrient absorption, improve intestinal physiological and ecological balance, and protect the intestinal mucosa to maintain normal gastrointestinal tract functions and avoid intestinal mucosal atrophy and intestinal bacterial translocation, which cause ectopic perioperative infections. Maintenance of the gut barrier is key to preventing severe insult-induced systemic inflammation and infection (19,20).

Similar to our results, Ding *et al.* proved that preoperative EN improved postoperative nutritional status and immune function, alleviated inflammatory response, and facilitated recovery for gastric cancer patients (21). Recently, novel modified techniques of enteral access have shown high success rates, low complication rates, and provided the benefits of minimal invasion even in patients with GOO (22-24). Endoscopic guidance and radiology help to traverse a compressed segment to deliver nutrients directly to the functional distal bowel (25). EN therapy is safe, effective, economical, and convenient, and has a wide range of applications in clinics (26,27).

PN is a necessary treatment for malnourished patients with absolute obstruction and may also prove useful to "top-up" nutrition in patients who cannot tolerate sufficient intake via the enteral route (28). Our study also assessed the length of preoperative PN therapy and found that after 3 d of preoperative PN treatment, the postoperative day of flatus passage reached to a relatively low

value, 4.8 d. With the prolongation of preoperative PN treatment, there is no association with time of postoperative flatus passage. Therefore, we propose that once patients can tolerate general anesthesia and surgery, there is no need to prolong the perioperative PN therapy.

The study is limited by its retrospective design and nonrandomized grouping. Another limitation is that the sample size was relatively small. Therefore, large-scale samples from multiple centers are required to confirm our findings.

Conclusions

Preoperative EN therapy would benefit gastric cancer patients with GOO by accelerating postoperative recovery. For patients with absolute obstruction, no more than 3-day PN therapy is recommended if patients can tolerate general anesthesia and surgery.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

References

- Fiori E, Lamazza A, Demasi E, et al. Endoscopic stenting for gastric outlet obstruction in patients with unresectable antro pyloric cancer. Systematic review of the literature and final results of a prospective study. The point of view of a surgical group. *Am J Surg* 2013;206:210-7.
- van Hooft JE, van Montfoort ML, Jeurnink SM, et al.

- Safety and efficacy of a new non-foreshortening nitinol stent in malignant gastric outlet obstruction (DUONITI study): a prospective, multicenter study. *Endoscopy* 2011;43:671-5.
- Storm AC, Ryou M. Advances in the endoscopic management of gastric outflow disorders. *Curr Opin Gastroenterol* 2017;33:455-60.
 - Keränen I, Kylänpää L, Udd M, et al. Gastric outlet obstruction in gastric cancer: a comparison of three palliative methods. *J Surg Oncol* 2013;108:537-41.
 - Marincaş AM, Prunoiu VM, Cirimbei C, et al. Digestive decompression to prevent digestive fistulas after gastric neoplasm resection. *Chirurgia (Bucur)* 2016;111:400-6.
 - O'Keefe SJ, Foody W, Gill S. Transnasal endoscopic placement of feeding tubes in the intensive care unit. *JPEN J Parenter Enteral Nutr* 2003;27:349-54.
 - Pronovost P, Needham D, Berenholtz S, et al. An intervention to decrease catheter-related bloodstream infections in the ICU. *N Engl J Med* 2006;355:2725-32.
 - Simpson F, Doig GS. Parenteral vs. enteral nutrition in the critically ill patient: a meta-analysis of trials using the intention to treat principle. *Intensive Care Med* 2005;31:12-23.
 - Reignier J, Boisramé-Helms J, Brisard L, et al. Enteral versus parenteral early nutrition in ventilated adults with shock: a randomised, controlled, multi-centre, open-label, parallel-group study (NUTRIR EA-2). *Lancet* 2018;391:133-43.
 - Braga M, Gianotti L, Gentilini O, et al. Early postoperative enteral nutrition improves gut oxygenation and reduces costs compared with total parenteral nutrition. *Crit Care Med* 2001;29:242-8.
 - Kondrup J, Rasmussen HH, Hamberg O, et al. Nutritional risk screening (NRS 2002): a new method based on an analysis of controlled clinical trials. *Clin Nutr* 2003;22:321-36.
 - Kernan WN, Viscoli CM, Brass LM, et al. Phenylpropanolamine and the risk of hemorrhagic stroke. *N Engl J Med* 2000;343:1826-32.
 - Sakurai K, Ohira M, Tamura T, et al. Predictive potential of preoperative nutritional status in long-term outcome projections for patients with gastric cancer. *Ann Surg Oncol* 2016;23:525-33.
 - van Hooft JE, Dijkgraaf MG, Timmer R, et al. Independent predictors of survival in patients with incurable malignant gastric outlet obstruction: a multicenter prospective observational study. *Scand J Gastroenterol* 2010;45:1217-22.
 - Chen HN, Chen XZ, Zhang WH, et al. The impact of body mass index on the surgical outcomes of patients with gastric cancer: A 10-year, single-institution cohort study. *Medicine (Baltimore)* 2015;94:e1769.
 - Rosania R, Chiapponi C, Malfertheiner P, et al. Nutrition in patients with gastric cancer: An update. *Gastrointest Tumors* 2016;2:178-87.
 - Sun K, Chen S, Xu J, et al. The prognostic significance of the prognostic nutritional index in cancer: a systematic review and meta-analysis. *J Cancer Res Clin Oncol* 2014;140:1537-49.
 - Moore FA, Feliciano DV, Andrassy RJ, et al. Early enteral feeding, compared with parenteral, reduces postoperative septic complications. The results of a meta-analysis. *Ann Surg* 1992;216:172-83.
 - Okamoto K, Fukatsu K, Hashiguchi Y, et al. Lack of preoperative enteral nutrition reduces gut-associated lymphoid cell numbers in colon cancer patients: a possible mechanism underlying increased postoperative infectious complications during parenteral nutrition. *Ann Surg* 2013;258:1059-64.
 - Song GM, Tian X, Liang H, et al. Role of enteral immunonutrition in patients undergoing surgery for gastric cancer: A systematic review and meta-analysis of randomized controlled trials. *Medicine (Baltimore)* 2015;94:e1311.
 - Ding D, Feng Y, Song B, et al. Effects of preoperative and postoperative enteral nutrition on postoperative nutritional status and immune function of gastric cancer patients. *Turk J Gastroenterol* 2015;26:181-5.
 - Ye P, Zeng L, Sun F, et al. A new modified technique of laparoscopic needle catheter jejunostomy: a 2-year follow-up study. *Ther Clin Risk Manag* 2016;12:103-8.
 - Iwase R, Suzuki Y, Yamanouchi E, et al. Double percutaneous transesophageal gastrotubing for gastric cancer: A pilot study. *J Surg Res* 2018;232:470-4.
 - O'Keefe S, Rolniak S, Raina A, et al. Enteral feeding patients with gastric outlet obstruction. *Nutr Clin Pract* 2012;27:76-81.
 - Chen ZH, Lin SY, Dai QB, et al. The effects of pre-

- operative enteral nutrition from nasal feeding tubes on gastric outlet obstruction. *Nutrients* 2017; 9:373.
26. Li B, Liu HY, Guo SH, et al. The postoperative clinical outcomes and safety of early enteral nutrition in operated gastric cancer patients. *J BUON* 2015; 20:468-72.
27. Reintam Blaser A, Starkopf J, Alhazzani W, et al. Early enteral nutrition in critically ill patients:ESICM clinical practice guidelines. *Intensive Care Med* 2017;43:380-98.
28. O'Keefe SJ. A guide to enteral access procedures and enteral nutrition. *Nat Rev Gastroenterol Hepatol* 2009;6:207-15.

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Table S1 Test for interactions (continuous variables)

Model	PN group [β (95% CI)]	P	EN group [β (95% CI)]	P	P interaction
Age (year)					
Crude	0.012 (-0.009, 0.033)	0.2511	0.013 (-0.016, 0.043)	0.3694	0.9521
Model I	0.009 (-0.011, 0.029)	0.3823	0.029 (0, 0.058)	0.0488	0.2324
Model II	0.005 (-0.016, 0.027)	0.6270	0.022 (-0.015, 0.058)	0.2420	0.3582
BMI (kg/m ²)					
Crude	-0.090 (-0.184, 0.004)	0.0626	0.043 (-0.114, 0.200)	0.5913	0.1494
Model I	-0.023 (-0.115, 0.069)	0.6292	0.117 (-0.034, 0.268)	0.1329	0.1046
Model II	0.023 (-0.077, 0.123)	0.6489	0.105 (-0.093, 0.303)	0.3001	0.3824
No solid food (d)					
Crude	0.015 (-0.004, 0.034)	0.1198	0.019 (-0.018, 0.056)	0.3189	0.8639
Model I	0.005 (-0.013, 0.024)	0.5723	0.020 (-0.021, 0.061)	0.3442	0.5049
Model II	0.001 (-0.025, 0.027)	0.9386	-0.002 (-0.050, 0.047)	0.9488	0.9101
Tumor size (cm)					
Crude	-0.024 (-0.140, 0.092)	0.6854	0.048 (-0.171, 0.266)	0.6692	0.5644
Model I	0.072 (-0.037, 0.181)	0.1980	0.115 (-0.096, 0.327)	0.2884	0.7079
Model II	0.064 (-0.054, 0.181)	0.2925	0.146 (-0.137, 0.430)	0.3142	0.5226
Financial costs (CNY)					
Crude	0	0.0530	0	0.1095	0.2689
Model I	0	0.0907	0	0.2159	0.4025
Model II	0	0.0866	0	0.6086	0.8794
Estimated blood loss (mL)					
Crude	0 (-0.001, 0.002)	0.4157	0.002 (-0.001, 0.004)	0.1442	0.3648
Model I	0 (-0.001, 0.001)	0.8402	0.001 (-0.001, 0.003)	0.1992	0.2793
Model II	0 (-0.001, 0.001)	0.9956	0.001 (-0.001, 0.003)	0.4170	0.3751
Nasogastric tube (POD)					
Crude	0.489 (0.259, 0.720)	0.0001	0.354 (-0.116, 0.824)	0.1462	0.5989
Model I	0.464 (0.257, 0.671)	<0.0001	0.190 (-0.215, 0.595)	0.3632	0.1817
Model II	0.539 (0.168, 0.911)	0.0173	-0.048 (-0.856, 0.760)	0.9103	0.0099
Drainage (POD)					
Crude	0.159 (0.110, 0.209)	<0.0001	0.260 (0.129, 0.391)	0.0002	0.1550
Model I	0.130 (0.083, 0.177)	<0.0001	0.323 (0.121, 0.526)	0.0022	0.0559
Model II	0.048 (-0.025, 0.121)	0.2053	0.234 (-0.079, 0.547)	0.1462	0.1713

Model I adjusts for preoperative nutritional therapy time, diabetes and T; Model II adjusts for preoperative nutritional therapy time, diabetes, Borrmann type, degree of histologic differentiation, T, N, complication and radical operation. PN, parenteral nutrition; EN, enteral nutrition; BMI, body mass index; POD, postoperative day; β , effect size; 95% CI, 95% confidence interval.

Table S2 Test for interactions (binomial and categorical variables)

Variables	Group	Crude [β (95% CI)]	P	Model I [β (95% CI)]	P	Model II [β (95% CI)]	P
Sex							
Male	PN	Ref.		Ref.		Ref.	
Female	PN	0.194 (-0.425, 0.813)	0.5405	0.224 (-0.376, 0.825)	0.4654	-0.133 (-0.715, 0.448)	0.6548
Male	EN	-0.835 (-1.501, -0.169)	0.0153	-0.491 (-1.146, 0.164)	0.1439	-0.305 (-0.938, 0.328)	0.3476
Female	EN	-0.994 (-1.797, -0.190)	0.0166	-0.723 (-1.504, 0.058)	0.0719	-0.411 (-1.152, 0.331)	0.2804
P interaction		0.5277		0.3770		0.9521	
NRS score							
3	PN	Ref.		Ref.		Ref.	
4	PN	-0.077 (-0.699, 0.544)	0.8074	0.285 (-0.340, 0.910)	0.3738	0.004 (-0.634, 0.643)	0.9895
5	PN	-0.212 (-1.368, 0.945)	0.7200	0.556 (-0.863, 1.975)	0.4438	0.743 (-0.620, 2.106)	0.2883
3	EN	-1.059 (-1.714, -0.404)	0.0019	-0.781 (-1.420, -0.141)	0.0182	-0.394 (-1.048, 0.259)	0.2399
4	EN	-1.033 (-1.949, -0.118)	0.0286	0.019 (-0.957, 0.994)	0.9701	-0.021 (-0.988, 0.946)	0.9656
5	EN	1.217 (-1.703, 4.136)	0.4155	1.420 (-1.265, 4.105)	0.3019	1.649 (-0.745, 4.044)	0.1802
P interaction		0.2926		0.3768		0.5054	
MIS							
No	PN	Ref.		Ref.		Ref.	
Yes	PN	-0.026 (-0.602, 0.551)	0.9309	-0.236 (-0.820, 0.349)	0.4309	-0.175 (-0.752, 0.402)	0.5530
No	EN	-1.088 (-1.749, -0.427)	0.0016	-0.799 (-1.464, -0.134)	0.0201	-0.396 (-1.016, 0.223)	0.2128
Yes	EN	-0.671 (-1.596, 0.254)	0.1571	-0.643 (-1.522, 0.235)	0.1538	-0.319 (-1.192, 0.555)	0.4763
P interaction		0.4427		0.4635		0.5977	
Reconstruction							
Billroth I	PN	Ref.		Ref.		Ref.	
Billroth II	PN	-0.552 (-1.398, 0.295)	0.2044	-0.118 (-0.994, 0.758)	0.7927	0.241 (-0.691, 1.174)	0.6133
Roux-en-Y	PN	-1.043 (-1.913, -0.173)	0.0206	-0.733 (-1.647, 0.181)	0.1193	-0.476 (-1.429, 0.476)	0.3301
Billroth I	EN	-1.600 (-3.004, -0.196)	0.0276	-0.762 (-2.189, 0.664)	0.2975	-0.205 (-1.546, 1.136)	0.7655
Billroth II	EN	-1.400 (-2.339, -0.461)	0.0042	-0.534 (-1.577, 0.509)	0.3178	-0.265 (-1.347, 0.817)	0.6326
Roux-en-Y	EN	-1.708 (-2.738, -0.678)	0.0015	-0.918 (-2.029, 0.193)	0.1085	-0.582 (-1.700, 0.537)	0.3111
P interaction		0.5251		0.7663		0.6588	
Tumor location							
Distal	PN	Ref.		Ref.		Ref.	
Middle	PN	-0.610 (-1.374, 0.154)	0.1199	-0.373 (-1.139, 0.394)	0.3424	-0.448 (-1.184, 0.288)	0.2354
Distal	EN	-1.118 (-1.708, -0.528)	0.0003	-0.765 (-1.363, -0.168)	0.0133	-0.427 (-1.009, 0.156)	0.1545
Middle	EN	-0.845 (-1.853, 0.162)	0.1024	-0.537 (-1.517, 0.443)	0.2851	-0.348 (-1.264, 0.569)	0.4592
P interaction		0.1861		0.3322		0.3096	
M							
M0	PN	Ref.		Ref.		Ref.	
M1	PN	-0.212 (-1.046, 0.622)	0.6194	-0.106 (-1.097, 0.885)	0.8342	-0.352 (-1.492, 0.789)	0.5470
M0	EN	-0.827 (-1.410, -0.245)	0.0062	-0.437 (-1.037, 0.162)	0.1554	-0.204 (-0.765, 0.356)	0.4767
M1	EN	-1.727 (-2.662, -0.792)	0.0004	-1.364 (-2.297, -0.431)	0.0049	-1.041 (-2.079, -0.003)	0.0523
P interaction		0.2970		0.2096		0.4619	

Model I adjusts for preoperative nutritional therapy time, diabetes and T; Model II adjusts for preoperative nutritional therapy time, diabetes, Borrmann type, degree of histologic differentiation, T, N, complication and radical operation. PN, parenteral nutrition; EN, enteral nutrition; NRS, nutritional risk screening; MIS, minimally invasive surgery; β , effect size; 95% CI, 95% confidence interval.