Original Article

Lack of clinical benefit from preoperative short-term parenteral nutrition on the clinical prognosis of patients treated with radical gastrectomy for gastric cancer: a two-center retrospective study based on propensity score matching analysis

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Background: Preoperative nutritional support studies for patients undergoing gastrointestinal (GI) surgery mostly focused on enteral nutrition (EN) or long-term (≥7 days) parenteral nutrition (PN). Some studies also found that preoperative short-term PN could improve the postoperative short-term nutritional status of tumor patients. But whether short-term PN support (1–6 days) before surgery can improve the prognosis of patients undergoing surgery for gastric cancer (GC) remains unclear. Therefore, we focused on assessing the effect of preoperative short-term PN on the outcomes of patients undergoing radical surgery for GC.

Methods: A retrospective analysis of 1,155 patients who underwent radical gastrectomy for GC between July 2014 and February 2019 was conducted. According to whether patients received short-term (1–6 days) PN support before surgery, patients were divided into non-PN group and PN group. After 1:1 propensity score matching (PSM), two groups of patients with similar baseline clinical characteristics were obtained. The incidence of various complications and overall survival (OS) rate were compared between the two groups, and logistic regression analysis for complications, Cox regression analysis for OS, and subgroup analysis were performed.

Results: Each group had 478 patients after PSM, and the clinical characteristics were balanced. There were no significant differences in overall postoperative complications (pre-PSM: P=0.495; post-PSM: P>0.99), postoperative length of stay (LOS; pre-PSM: P=0.092; post-PSM: P=0.460), or readmission rate within 30 days (pre-PSM: P=0.496; post-PSM: P=0.793) between the two groups before and after PSM. The OS of PN group before matching was lower than that of non-PN group (P=0.023), but this difference was not significant after matching (P=0.950), but the PN group's hospitalization expenses were substantially greater than those of the control group (post-PSM: P<0.001). Preoperative short-term PN support was not an

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independent factor in the incidence of postoperative complications (P>0.99) and OS (P=0.949). Subgroup analyses failed to identify those patients who might benefit from preoperative short-term PN support.
Conclusions: Preoperative short-term PN support may have no significant benefit on short-term postoperative complications or the long-term OS of patients with GC but increase hospitalization costs. It thus should not be the first choice of treatment for these patients.

Keywords: Gastric cancer (GC); parenteral nutrition (PN); postoperative complications; propensity score matching (PSM); survival time

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Introduction

Gastric cancer (GC), which ranks as the fifth most frequently diagnosed cancer and the fourth most frequent cause of cancer-related death worldwide (1), is a major contributor to the global burden of disability-adjusted life years, especially in East Asia, where both the incidence rates (32.1/100,000 for men; 13.2/100,000 for women) and mortality rates (15.9/100,000) are the highest (2,3). Surgery is the optimal choice for GC, but it is associated with high rates of postoperative complications and mortality (2). Effectively improving the prognosis of patients treated with surgery for GC has thus become an urgent and challenging issue. Many studies have identified factors that predict postoperative complications, including indicators based on body constitution, nutrition, inflammation, organ function, and hypercoagulation (4,5). Effectively improving the prognosis of patients treated with surgery for GC has thus become an urgent and challenging issue. A study has demonstrated that nutritional support can be used in conjunction with anticancer therapy to increase patients' resistance to treatment (6). Patients with gastrointestinal (GI) tumors have an increased risk of malnutrition due to factors such as hypermetabolism, digestive and absorption dysfunction, and inflammatory response (7). Nutrition is crucial to improving the prognosis of patients after abdominal major surgery, particularly those with malnutrition and other issues affecting nutrition (8-15). It has been reported that nutritional support can improve body composition, muscle strength, weight, and reduce chemotherapy toxicity (16,17). Macronutrients such as fatty acids or amino acids and micronutrient components such as vitamin D also have anti-inflammatory properties (18).

Enteral nutrition (EN) and parenteral nutrition (PN) are supplements to oral diets that are administered to meet the nutritional needs of patients who lack adequate oral intake (19). The European Society for Parenteral and Enteral Nutrition (ESPEN) recommends EN for patients with cancer (20). In addition, as opposed to EN, PN is less commonly used by surgeons because it is less incompatible with human physiology (6). Studies have shown that the prevalence of postoperative complications decreases in malnourished patients with longer preoperative PN (≥7 days) (9), whereas it did not decrease with short-term PN (21,22). In fact, patients receiving PN therapy are not limited to those who are malnourished. The effect of short-term PN on the clinical prognosis of non-malnourished patients undergoing abdominal surgery is unknown, especially on long-term survival. Therefore, in this study, we investigated the short- and long-term prognosis of patients with GC undergoing radical surgery after receiving preoperative short-term PN support. We present

Highlight box

Key findings
- Preoperative short-term parenteral nutrition (PN) does not benefit clinical outcomes of patients treated with radical gastrectomy for gastric cancer (GC).

What is known and what is new?
- Preoperative long-term PN can improve the prognosis of abdominal surgery.
- Preoperative short-term PN support has no significant benefit on short-term postoperative complications or the long-term survival of patients with GC and may increase hospitalization costs.

What is the implication, and what should change now?
- Surgeons should carefully consider the necessity of preoperative PN and its duration in patients with an oral diet.

this article in accordance with the STROBE reporting checklist (available at https://jgo.amegroups.com/article/view/10.21037/jgo-23-1000/rc).

Methods

Patients

We retrospectively collected data of patients with GC who underwent surgery in the First Affiliated Hospital of Wenzhou Medical University and the Second Affiliated Hospital of Wenzhou Medical University in China from July 2014 to February 2019. In all cases, the following criteria were met: (I) age ≥18 years; (II) gastric adenocarcinoma confirmed by postoperative pathology; (III) undergoing radical gastrectomy; (IV) having abdominal computed tomography (CT) examination within 1 month prior to surgery; and (V) receiving no or only short-term PN (1–6 days) before surgery. We excluded patients with the following criteria: (I) lack of data required for analysis; (II) undergoing palliative or emergency surgery; (III) preoperative fasting due to illness; (IV) presence of severe immunologic, hematologic, or endocrine disease; and (V) GC concurrent with other malignancies. Finally, data from 1,155 patients, 557 of whom received short-term PN support before surgery, were included in the analysis.

Data collection

The following information was extracted from the medical record system or follow-up record for retrospective analysis: (I) basic clinical information, including age, gender, height, weight, Nutritional Risk Screening (NRS) 2002 score (23,24), Charlson comorbidity index (CCI) (25), preoperative hemoglobin level (with male hemoglobin <120 g/L or female <110 g/L considered to indicate anemia), and preoperative plasma albumin (<35 g/L was defined as hypoproteinemia); (II) tumor characteristics, including tumor histological classification, differentiation grade, and tumor-node-metastasis (TNM) staging [American Joint Committee on Cancer (AJCC) cancer staging system, eighth edition]; (III) surgical information, including surgical approach, extent of gastrectomy, method of digestive tract reconstruction mode, and combined organ resection; and (IV) prognosis, including postoperative complications, surgical mortality (death within 30 days after surgery), length of stay (LOS) following surgery, readmission rate within 1 month, long-term survival time, and total hospitalization costs. According to the Clavien-Dindo classification system, we included complications of grade II or higher in the analysis and defined severe complications as those of grade III or higher (26). After discharge, patients should have regular outpatient follow-up according to the doctor's advice. If no outpatient records were found or the frequency was too low, telephone follow-up should be conducted. Within 2 years of discharge, patients were followed every 3 months and then every 6 months between 3 and 5 years after discharge until they lost contact or died.

Measurement of muscle mass

CT images of the lower edge of the third lumbar spine vertebra (L3) obtained from each patient within 1 month before surgery were saved. Two trained researchers used a specialized processing system (ImageJ; version 1.48V; Java 1.6.0-20; 64 bits; National Institutes of Health, Bethesda, MD, USA), all the skeletal muscles were delineated in Hounsfield units (HU) ranging from −29 to 150, and their areas were calculated. Subsequently, we divided muscle area by the square of height (m^2) to obtain the L3 skeletal muscle index (SMI; cm^2/m^2). Based on our previous study, L3 SMI <34.9 cm^2/m^2 in females or SMI <40.8 cm^2/m^2 in males indicated a reduced muscle mass (low SMI) (27).

Preoperative nutrition support

Based on whether they received PN prior to surgery, the patients were divided into a non-PN group and a PN group. In the non-PN group, the normal hospital oral diet, including the special diet, was administered. The PN group received PN containing at least amino acids, glucose, and lipid emulsion for 1–6 days through a peripheral or central vein and could also include electrolytes, vitamins, and trace elements as a nutritional supplement to an oral diet (28).

Propensity score matching (PSM)

PSM is a statistical technique that employs intervention effect analysis in observational studies to lessen data bias and account for the confounding variables between groups. In order to increase the balance between groups, we used age, SMI, body mass index (BMI), NRS 2002 score, CCI, preoperative hemoglobin level, preoperative albumin level, tumor growth location, degree of differentiation, and TNM stage as matching factors, which may be variables that affect clinicians in making nutritional support decisions. PSM was implemented in a 1:1 proportion with the closest neighbor coordinating technique and a caliper of 0.02 being used to avoid mismatches.

Statistical analysis

All continuous data, including that of BMI, postoperative LOS, and hospital costs, were nonnormally distributed as determined by the Kolmogorov-Smirnov test. Consequently, the Mann-Whitney test was used to compare data between groups using the median and interquartile range (IQR). The Fisher exact or Pearson chi-squared tests were employed to compare categorical data, while the rank-sum test was applied for ordinal variables. Univariate analysis was used to examine the potential risk factors associated with complications or overall survival (OS). Variables with P<0.05 (two-tailed) were considered statistically significant, and results were subsequently presented as odds ratio (OR) or hazard ratio (HR) with 95% confidence intervals (CIs) in multivariate logistic or Cox regression analyses, respectively, using a "forward: LR" approach. Survival curves were compared using Kaplan-Meier analysis, and significance was determined using the log-rank test. P values <0.05 were considered statistically significant. SPSS software (version 25.0; IBM Corp., Armonk, NY, USA) was used to perform statistical analyses.

Ethical disclosure

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the ethics committee of the First Affiliated Hospital of Wenzhou Medical University (No. KY2022-202), and the Second Affiliated Hospital of Wenzhou Medical University was informed and agreed to this study. Individual consent for this retrospective analysis was waived.

Results

Demographic and therapeutic characteristics

A total of 1,155 patients were enrolled in this study, 557 (48.2%) of whom received short-term PN support before surgery. After PSM, a total of 478 patients were included in each group, and *Table 1* lists the demographic and therapeutic characteristics before and after PSM. We found that patients in the PN group were older (age ≥70 years: 29.3% *vs.* 35.7%, P=0.019), had lower muscle mass (16.2% *vs.* 22.6%, P=0.006), higher nutritional risk (P<0.001), lower hemoglobin (26.3% *vs.* 38.1%, P<0.001), and albumin (15.7% *vs.* 23.5%, P=0.001). In addition, the PN group had deeper tumor invasion (T stage; P<0.001), more lymph node metastasis (N stage; P=0.047), and later phenomenon of TNM stage (P<0.001). There were no significant differences in gender, CCI, surgical approach, extent of resection, combined organ resection, or tumor location and differentiation between the two groups. The differences between the two groups were well homogenized after PSM.

Comparison of postoperative short-time outcomes between the PN group and non-PN group

As shown in *Table 2*, in the comparison of postoperative outcomes between the PN and non-PN groups, it was observed that hospitalization costs were higher in the PN group both before and after matching (pre-PSM: P<0.001; post-PSM: P<0.001), but there was no statistically significant in postoperative LOS (pre-PSM: P=0.092; post-PSM: P=0.460) or readmission rate within 30 days (pre-PSM: P=0.496; post-PSM P=0.793). In the analysis of postoperative complications, there was no statistical significance between the two groups in the incidence of total complications (pre-PSM: P=0.495; post-PSM: P>0.99) or infectious (pre-PSM: P=0.130; post-PSM: P=0.513) or noninfectious complications (pre-PSM: P=0.891; post-PSM: P=0.474). However, it was worth mentioning that anastomotic fistulas were more common in the PN group than in the non-PN group (pre-PSM: P=0.019; post-PSM, P=0.031).

Subgroup analysis was then conducted on the influence of preoperative short-term PN support in order to identify potential beneficiaries, but unfortunately, our results (*Figure 1*) showed that short-term PN support did not demonstrate meaningful effectiveness in the subgroups, including in those of age, gender, NRS 2002 score, CCI, anemia, hypoalbuminemia, surgical method, and tumor TNM stage.

Comparison of OS between the PN group and non-PN group

We further explored whether preoperative short-term PN had an impact on OS (*Figure 2*). As shown in *Figure 2A*, before the PSM, the PN group had a lower OS rate than did the non-PN group (P=0.023), but this difference disappeared after matching (P=0.950). In addition, we

Table 1 Patient characteristics of the non-PN and PN groups

Factors	All patients			After matching		
	Non-PN group (n=598)	PN group (n=557)	P	Non-PN group (n=478)	PN group (n=478)	P
BMI (kg/m^2)	22.3 (20.4–24.3)	22.3 (20.4–24.5)	0.99	22.6 (20.6–24.6)	22.4 (20.4–24.5)	0.542
Age (years)			0.019*			0.451
<70	423 (70.7)	358 (64.3)		321 (67.2)	323 (67.6)	
≥70	175 (29.3)	199 (35.7)		166 (34.7)	155 (32.4)	
Gender			0.253			0.428
Female	177 (29.6)	148 (26.6)		139 (29.1)	128 (26.8)	
Male	421 (70.4)	409 (73.4)		339 (70.9)	340 (71.1)	
Low SMI			0.006*			0.741
No	501 (83.8)	431 (77.4)		390 (81.6)	386 (80.8)	
Yes	97 (16.2)	126 (22.6)		88 (18.4)	92 (19.2)	
NRS 2002 score			<0.001*			0.470
1–2	456 (76.3)	357 (64.1)		339 (70.9)	327 (68.4)	
3–4	112 (18.7)	162 (29.1)		109 (22.8)	124 (25.9)	
5–6	30 (5.0)	38 (6.8)		30 (6.3)	27 (5.6)	
CCI			0.504			0.642
0	360 (60.2)	330 (59.2)		281 (58.8)	290 (60.7)	
1	163 (27.3)	141 (25.3)		127 (26.6)	117 (24.5)	
2–6	75 (12.5)	86 (15.4)		70 (14.6)	71 (14.9)	
Preoperative anemia			<0.001*			0.944
No	441 (73.7)	345 (61.9)		331 (69.2)	332 (69.5)	
Yes	157 (26.3)	212 (38.1)		147 (30.8)	146 (30.5)	
Preoperative hypoalbuminemia			0.001*			0.456
No	504 (84.3)	426 (76.5)		384 (80.3)	393 (82.2)	
Yes	94 (15.7)	131 (23.5)		94 (19.7)	85 (17.8)	
Scope of gastrectomy			0.233			0.892
Partial	399 (66.7)	353 (63.4)		308 (64.4)	170 (35.6)	
Total	199 (33.3)	204 (36.6)		310 (64.9)	168 (35.1)	
Laparoscopy			0.082			0.302
No	390 (65.2)	390 (70.0)		313 (65.5)	328 (68.6)	
Yes	208 (34.8)	167 (30.0)		165 (34.5)	150 (31.4)	
Combined organ excision			0.894			0.561
No	568 (95.0)	530 (95.2)		451 (94.4)	455 (95.2)	
Yes	30 (5.0)	27 (4.8)		27 (5.6)	23 (4.8)	

Table 1 (*continued*)

Table 1 (*continued*)

Factors	All patients			After matching		
	Non-PN group (n=598)	PN group (n=557)	P	Non-PN group (n=478)	PN group (n=478)	P
Tumor location			0.290			0.298
Pylorus	373 (62.4)	353 (63.4)		293 (61.3)	299 (62.6)	
Body	133 (22.2)	129 (23.2)		111 (23.2)	113 (23.6)	
Cardia	85 (14.2)	63 (11.3)		68 (14.2)	54 (11.3)	
Linitis plastica	7 (1.2)	12 (2.2)		6 (1.3)	12 (2.5)	
Degree of tumor differentiation			0.435			0.540
Well-differentiated	68 (11.4)	52 (9.3)		57 (11.9)	51 (10.7)	
Moderately differentiated	129 (21.6)	122 (21.9)		104 (21.8)	102 (21.3)	
Poorly differentiated	401 (67.1)	383 (68.8)		317 (66.3)	325 (68.0)	
T stage			<0.001*			0.199
1	230 (38.5)	144 (25.9)				
2	83 (13.9)	89 (16.0)		62 (13.0)	83 (17.4)	
3	47 (7.9)	31 (5.6)		37 (7.7)	27 (5.6)	
4	238 (39.8)	293 (52.6)		209 (43.7)	224 (46.9)	
N stage			0.047*			0.383
0	323 (54.0)	255 (45.8)		254 (53.1)	230 (48.1)	
1	77 (12.9)	89 (16.0)		62 (13.0)	79 (16.5)	
2	82 (13.7)	115 (20.6)		71 (14.9)	88 (18.4)	
3	116 (19.4)	98 (17.6)		91 (19.0)	81 (16.9)	
TNM stage			<0.001*			0.325
I	272 (45.5)	184 (33.0)		202 (42.3)	182 (38.1)	
II	108 (18.1)	132 (23.7)		92 (19.2)	105 (22.0)	
III	218 (36.5)	241 (43.3)		184 (38.5)	191 (40.0)	

Values are presented as median (IQR) or n (%). *, P<0.05, indicating statistical significance. PN, parenteral nutrition; BMI, body mass index; SMI, skeletal muscle index; NRS 2002, Nutritional Risk Screening 2002; CCI, Charlson comorbidity index; TNM, tumor-node-metastasis; IQR, interquartile range.

found that the survival of low-SMI patients was lower than that of normal SMI patients (*Figure 2B₁*, P=0.018), but in the subgroup analysis, preoperative short-term PN had no obvious effect on the survival of any of the groups (*Figure 2B₂*; non-low SMI group: P=0.820; low SMI group: P=0.700). Similarly, survival rates differed significantly across patients with different TNM stages (P<0.0001) or different degrees of tumor differentiation (P<0.0001), but these differences were not apparent in the subgroup analysis (*Figure 2C,2D*).

Risk factors for postoperative complications and OS

Multivariate logistic analysis was used to determine factors associated with overall postoperative complications (*Table 3*). Univariate analysis showed that low SMI (P=0.020), age ≥70 years (P=0.003), higher CCI (P=0.007), preoperative anemia (P<0.001), hypoalbuminemia (P=0.006), laparoscopic surgery (P<0.001) and the digestive tract reconstruction method (P=0.001) were substantially correlated with total postoperative complications. After these factors were

Table 2 Comparison of postoperative outcomes between the non-PN and PN groups

Factors	All patients			After matching		
	Non-PN group (n=598)	PN group (n=557)	P value	Non-PN group (n=478)	PN group (n=478)	P value
Postoperative LOS (days)	13.0 (11.0–16.1)	13.0 (11.0–18.1)	0.092	13.0 (11.0–17.0)	13.0 (11.0–18.1)	0.460
Hospitalization cost[†] (¥)	55,872.3 (48,897.2–65,283.1)	60,564.6 (52,161.9–73,429.2)	<0.001*	55,953.1 (48,337.3–66,538.0)	59,709.6 (51,452.9–72,971.4)	<0.001*
Readmission within 30 days	39 (6.5)	31 (5.6)	0.496	32 (6.7)	30 (6.3)	0.793
Total complications[‡]	140 (23.4)	140 (25.1)	0.495	119 (24.9)	119 (24.9)	>0.99
Clavien-Dindo grade			0.427			0.886
Grade II	90 (15.1)	84 (15.1)		79 (16.5)	71 (14.9)	
Grade III	39 (6.5)	40 (7.2)		31 (6.5)	38 (7.9)	
Grade IV	11 (1.8)	12 (2.2)		9 (1.9)	9 (1.9)	
Grade V	0 (0.0)	3 (0.5)		0 (0.0)	1 (0.2)	
Infective complications	70 (11.7)	82 (14.7)	0.130	63 (13.2)	70 (14.6)	0.513
Intra-abdominal infection	28 (4.7)	41 (7.4)	0.055	27 (5.6)	35 (7.3)	0.293
Anastomotic leakage	4 (0.7)	13 (2.3)	0.019*	3 (0.6)	11 (2.3)	0.031*
Duodenal stump leakage	1 (0.2)	4 (0.7)	0.202	1 (0.2)	4 (0.8)	0.374
Incision infection	12 (2.0)	14 (2.5)	0.562	11 (2.3)	14 (2.9)	0.543
Pancreatic fistula	1 (0.2)	4 (0.7)	0.202	1 (0.2)	4 (0.8)	0.374
Pulmonary infections	33 (5.5)	27 (4.8)	0.608	28 (5.9)	22 (4.6)	0.383
Sepsis	0 (0.0)	3 (0.5)	0.112	0 (0.0)	2 (0.4)	0.499
Urinary infection	0 (0.0)	3 (0.5)	0.112	0 (0.0)	2 (0.4)	0.499
Septic shock	0 (0.0)	3 (0.5)	0.112	0 (0.0)	3 (0.6)	0.249
Noninfective complications	93 (15.6)	85 (15.3)	0.891	78 (16.3)	70 (14.6)	0.474
Intra-abdominal bleeding	21 (3.5)	16 (2.9)	0.538	17 (3.6)	12 (2.5)	0.346
Gastroparesis	10 (1.7)	12 (2.2)	0.549	10 (2.1)	9 (1.9)	0.817
Intestinal obstruction	18 (3.0)	11 (2.0)	0.261	17 (3.6)	8 (1.7)	0.068
Pleural effusion	12 (2.0)	12 (2.2)	0.860	10 (2.1)	9 (1.9)	0.817
Peritoneal effusion	4 (0.7)	5 (0.9)	0.746	1 (0.2)	4 (0.8)	0.374
Deep venous thrombosis	8 (1.3)	7 (1.3)	0.903	6 (1.3)	7 (1.5)	0.780
Respiratory failure	2 (0.3)	3 (0.5)	0.677	2 (0.4)	3 (0.6)	>0.99
Cardiac insufficiency	2 (0.3)	3 (0.5)	0.677	2 (0.4)	3 (0.6)	>0.99
Hypohepatia	3 (0.5)	8 (1.4)	0.102	3 (0.6)	7 (1.5)	0.204
Renal insufficiency	1 (0.2)	1 (0.2)	>0.99	1 (0.2)	1 (0.2)	>0.99
Multiple organ dysfunction syndrome	0 (0.0)	2 (0.4)	0.232	0 (0.0)	2 (0.4)	0.499
Lymphatic fistula	6 (1.0)	6 (1.1)	0.902	4 (0.8)	5 (1.0)	>0.99
Others	7 (1.2)	6 (1.1)	0.881	5 (1.0)	4 (0.8)	>0.99
Death	0 (0.0)	3 (0.5)	0.112	0 (0.0)	1 (0.2)	>0.99

Values are presented as median (IQR) or n (%). [†], total complications were defined as complications classified as grade II or above; *, P<0.05, indicating statistical significance. PN, parenteral nutrition; LOS, length of stay; IQR, interquartile range.

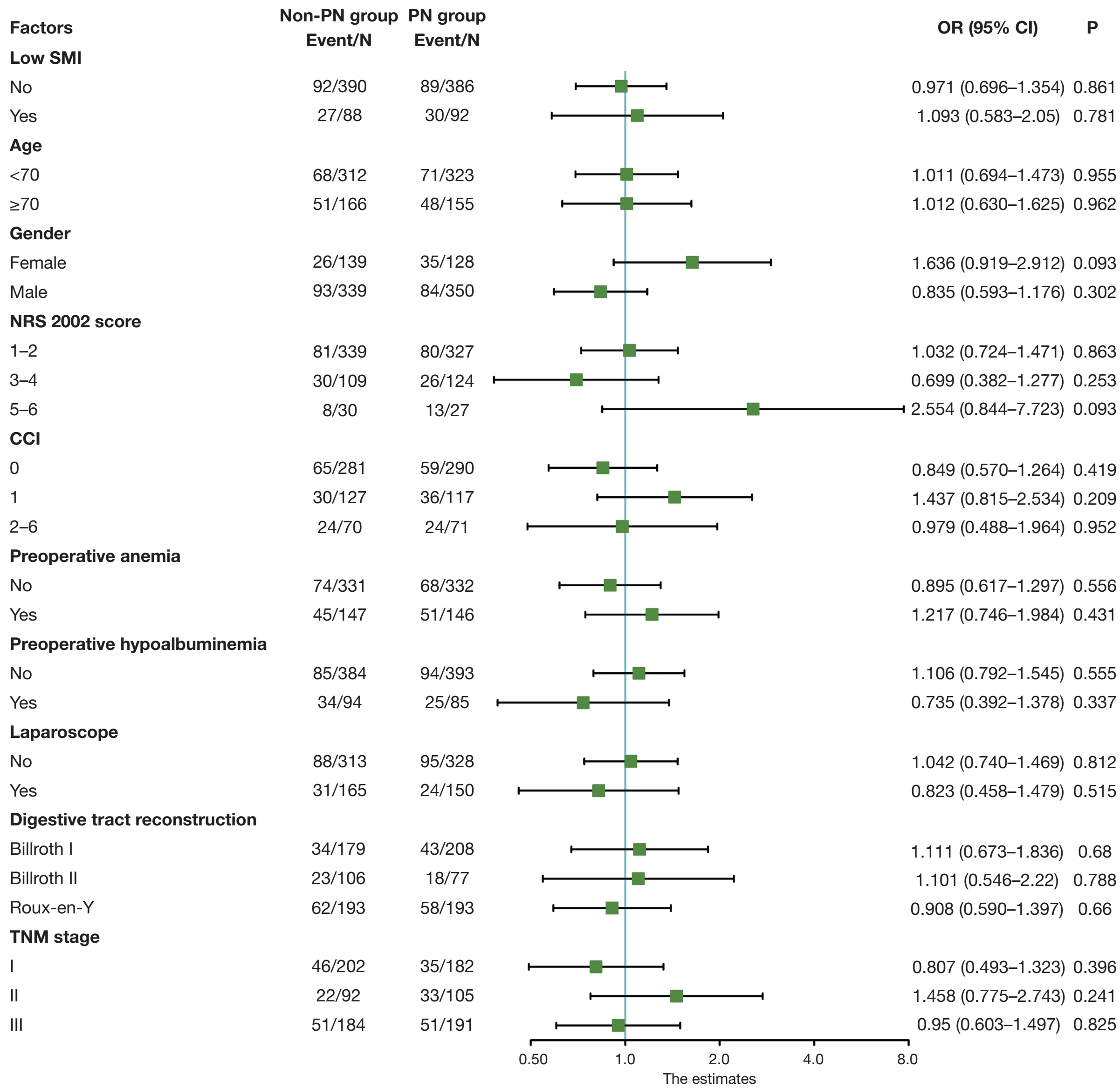

Figure 1 Subgroup analysis of postoperative complications. If not specifically stated, the values are presented as the number. PN, parenteral nutrition; OR, odds ratio; CI, confidence interval; SMI, skeletal muscle index; NRS 2002, Nutritional Risk Screening 2002; CCI, Charlson comorbidity index; TNM, tumor-node-metastasis.

incorporated into the subsequent multivariate analysis, age ≥70 years (P=0.043), higher CCI (P=0.012), preoperative anemia (P=0.004), laparoscopic surgery (P=0.002), and digestive tract reconstruction mode (P=0.005) were found to be independently associated with the incidence of postoperative complications in this study.

Cox analysis was used to determine the risk factors affecting postoperative OS (*Table 4*). Significant factors om univariate analysis including low SMI (P=0.019), age (P<0.001), NRS 2002 score (P=0.002), preoperative anemia (P<0.001), hypoalbuminemia (P<0.001), laparoscopic surgery (P<0.001), digestive tract reconstruction mode (P<0.001), combined organ excision (P<0.001), degrees of tumor differentiation (P<0.001), and TNM stage (P<0.001) were included in multifactor analysis, after which only age ≥70 years (P<0.001), laparoscopic surgery (P=0.008), digestive tract reconstruction mode (P<0.001), combined organ excision (P=0.031), and degree of differentiation (P=0.002),

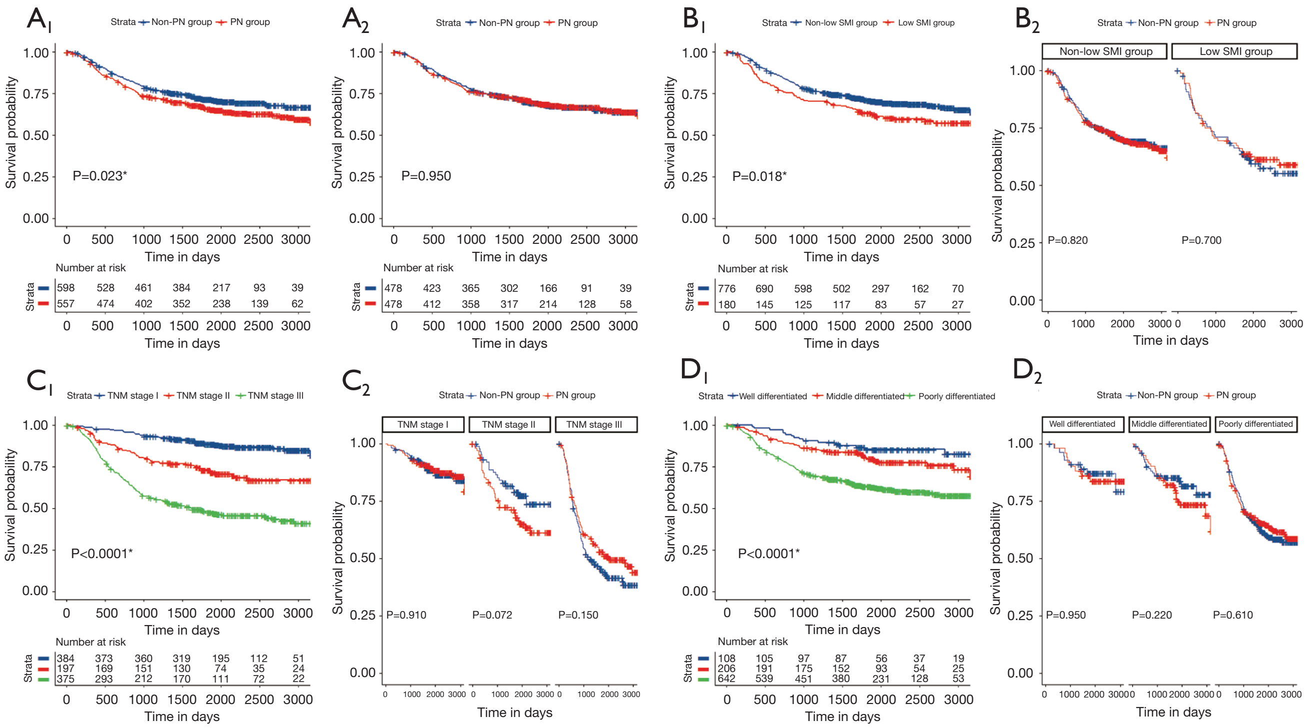

Figure 2 Long-term OS after surgery. (A_1) Comparison of OS between the non-PN and PN groups before PSM. (A_2) Comparison of OS between the non-PN and PN groups after PSM. (B_1) Comparison of OS between the non-low SMI and low-SMI groups after PSM. (B_2) Subgroup comparison of OS according to SMI. (C_1) Comparison of OS across the three TNM stages. (C_2) Subgroup comparison of OS according to TNM stage. (D_1) Comparison of OS across the three degrees of tumor differentiation. (D_2) Subgroup comparison of OS according to the degree of tumor differentiation. *, P<0.05, indicating statistical significance. PN, parenteral nutrition; SMI, skeletal muscle index; TNM, tumor-node-metastasis; OS, overall survival; PSM, propensity score matching.

and TNM stage (P<0.001) were found to affect OS.

Discussion

Patients with GC may have abnormalities such as elevated basal metabolic rate, carbohydrate metabolism, and protein metabolism (7). Surgery can cause a series of stress reactions, such as the release of cytokines, including stress hormones and inflammation mediators, that enhance glycogen, fat, and protein catabolism and release sufficient substrates to facilitate healing (29). These reactions lead to insulin resistance, immunosuppression, muscle mass loss, and other adverse effects (30). Proper nutrition can provide adequate raw materials and mobilize the required substrates for anabolism during rapid convalescence (31). The main goal of perioperative nutritional therapy is to enable patients to obtain adequate energy reserves in the shortest time; to better maintain muscle mass, immunity, and cognitive function by avoiding starvation; and to facilitate postoperative recovery from surgical trauma and possible infections. Compared with PN, EN is favored by many nutritionists and surgeons because the way of absorption and utilization of nutrients is more in line with human physiology and helps to maintain the integrity of the intestinal mucosal structure and barrier function (6). Although oral intake is the preferred form of nutritional intake, PN is needed to provide nutritional support for patients with upper GI cancer who experience nausea, vomiting, dysphagia, obstruction, and other phenomena hindering eating. Therefore, preoperative PN nutrition is still extensively used.

A randomized open trial conducted by Sánchez-Guillén *et al.* (32) indicated that perioperative PN appeared to be statistically associated with fewer complications in patients with colorectal cancer (OR =0.2; 95% CI: 0.08–0.87), and a randomized clinical trial subanalysis by López-Rodríguez-Arias *et al.* (33) reported a 15% reduction in complications in patients with low SMI supported by peripheral PN,

Table 3 Univariate and multivariate logistic regression analysis for the prediction of total postoperative complications

Factors	Without complications (n=718)	With complications (n=238)	Univariate analysis		Multivariate analysis	
			OR (95% CI)	P value	OR (95% CI)	P value
Group				>0.99		
Non-PN group	359 (50.0)	119 (50.0)	1			
PN group	359 (50.0)	119 (50.0)	1.000 (0.746–1.341)			
Low SMI				0.020*		0.114
No	595 (82.9)	181 (76.1)	1			
Yes	123 (17.1)	57 (23.9)	1.523 (1.068–2.173)			
Age (years)				0.003*		0.043*
<70	496 (69.1)	139 (58.4)	1		1	
≥70	222 (30.9)	99 (41.6)	1.591 (1.176–2.153)		1.380 (1.010–1.886)	
Gender				0.362		
Female	206 (28.7)	61 (25.6)	1			
Male	512 (71.3)	177 (74.4)	1.167 (0.837–1.629)			
NRS 2002 score				0.105		
1–2	505 (70.3)	161 (67.6)	1			
3–4	177 (24.7)	56 (23.5)	0.992 (0.700–1.407)			
5–6	36 (5.0)	21 (8.8)	1.830 (1.038–3.225)			
CCI				0.007*		0.012*
0	447 (62.3)	124 (52.1)	1		1	
1	178 (24.8)	66 (27.7)	1.337 (0.946–1.888)		1.345 (0.943–1.918)	
2–6	93 (13.0)	48 (20.2)	1.861 (1.246–2.779)		1.815 (1.202–2.741)	
Preoperative hypoalbuminemia				0.006*		0.375
No	598 (83.3)	179 (75.2)	1			
Yes	120 (16.7)	59 (24.8)	1.643 (1.153–2.339)			
Preoperative anemia				<0.001*		0.004*
No	521 (72.6)	142 (59.7)	1		1	
Yes	197 (27.4)	96 (40.3)	1.788 (1.316–2.429)		1.605 (1.167–2.206)	
Laparoscope				<0.001*		0.002*
No	458 (63.8)	183 (76.9)	1		1	
Yes	260 (36.2)	55 (23.1)	0.529 (0.378–0.742)		0.580 (0.410–0.822)	
Digestive tract reconstruction mode				0.001*		0.005*
Billroth I	310 (43.2)	77 (32.4)	1		1	
Billroth II	142 (19.8)	41 (17.2)	1.162 (0.758–1.783)		0.969 (0.624–1.506)	
Roux-en-Y	266 (37.0)	120 (50.4)	1.816 (1.306–2.526)		1.639 (1.169–2.298)	

Table 3 (*continued*)

Table 3 (*continued*)

Factors	Without complications (n=718)	With complications (n=238)	Univariate analysis		Multivariate analysis	
			OR (95% CI)	P value	OR (95% CI)	P value
Combined organ excision				0.126		
No	685 (95.4)	221 (92.9)	1			
Yes	33 (4.6)	17 (7.1)	1.597 (0.872–2.922)			
Degrees of tumor differentiation				0.904		
Well-differentiated	83 (11.6)	25 (10.5)	1			
Moderately differentiated	154 (21.4)	52 (21.8)	1.121 (0.649–1.936)			
Poorly differentiated	481 (67.0)	161 (67.6)	1.111 (0.687–1.798)			
TNM stage				0.083		
I	303 (42.2)	81 (34.0)	1			
II	142 (19.8)	55 (23.1)	1.449 (0.975–2.153)			
III	273 (38.0)	102 (42.9)	1.398 (1.000–1.953)			

If not specifically stated, the values are presented as n (%). *, P<0.05, indicating statistical significance. OR, odds ratio; CI, confidence interval; PN, parenteral nutrition; SMI, skeletal muscle index; NRS 2002, Nutritional Risk Screening 2002; CCI, Charlson comorbidity index; TNM, tumor-node-metastasis.

Table 4 Univariate and multivariate Cox regression analysis for the prediction of OS

Factors	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P value	HR (95% CI)	P value
Group		0.949		
Non-PN group	1			
PN group	1.007 (0.805–1.261)			
Low SMI		0.019*		0.450
No	1			
Yes	1.374 (1.055–1.79)			
Age (years)		<0.001*		<0.001*
<70	1		1	
≥70	1.682 (1.341–2.11)		1.604 (1.274–2.02)	
Gender		0.084		
Female	1			
Male	1.261 (0.969–1.64)			
NRS 2002 score		0.002*		0.571
1–2	1			
3–4	1.318 (1.02–1.705)			
5–6	1.933 (1.292–2.892)			

Table 4 (*continued*)

Table 4 (*continued*)

Factors	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P value	HR (95% CI)	P value
CCI		0.558		
0	1			
1	1.039 (0.796–1.356)			
2–6	1.189 (0.869–1.628)			
Preoperative hypoalbuminemia		<0.001*		0.247
No	1			
Yes	1.858 (1.445–2.389)			
Preoperative anemia		<0.001*		0.073
No	1			
Yes	1.942 (1.548–2.437)			
Laparoscopy		<0.001*		0.008*
No	1		1	
Yes	0.498 (0.378–0.656)		0.684 (0.515–0.907)	
Digestive tract reconstruction		<0.001*		<0.001*
Billroth I	1		1	
Billroth II	1.888 (1.354–2.633)		1.256 (0.893–1.764)	
Roux-en-Y	2.575 (1.971–3.364)		1.727 (1.312–2.273)	
Combined organ excision		<0.001*		0.031*
No	1		1	
Yes	2.302 (1.57–3.375)		1.536 (1.041–2.267)	
Degrees of tumor differentiation		<0.001*		0.002*
Well differentiated	1		1	
Moderately differentiated	1.581 (0.893–2.797)		0.800 (0.44–1.453)	
Poorly differentiated	3.162 (1.906–5.245)		1.394 (0.807–2.408)	
TNM stage		<0.001*		<0.001*
I	1		1	
II	2.658 (1.807–3.908)		2.146 (1.433–3.213)	
III	5.996 (4.373–8.222)		4.275 (3.016–6.058)	

*, P<0.05, indicating statistical significance. OS, overall survival; HR, hazard ratio; CI confidence interval; PN, parenteral nutrition; SMI, skeletal muscle index; NRS 2002, Nutritional Risk Screening 2002; CCI, Charlson comorbidity index; TNM, tumor-node-metastasis.

but these were for perioperative PN (1 day prior to surgery to 3 days after surgery). A recent review focusing on perioperative nutrition in GI surgery demonstrated that there were insufficient studies on preoperative PN, especially randomized controlled clinical trials (32), and further studies will be beneficial to guiding clinical practice. Some studies have found that receiving long-term PN (≥7 days) before surgery reduces postoperative complications, especially malnutrition (11-14,34). In a prospective study, preoperative and total length of hospital stay were longer in the preoperative nutrition group (median LOS: 33 *vs.* 27 days, P<0.001) (35). Considering the actual situation of hospitals in China, only a few patients with GC clinically receive long-term preoperative nutritional support. Because few studies have investigated the effect of short-term intravenous nutrition interventions on clinical outcomes, the importance of preoperative short-term nutrition is unclear.

The effect of PN on patients with malnutrition has been demonstrated, however the effect on well-nourished patients has not been studied. Our data showed that there were also patients with better nutrition who received short-term PN. The incidence of true malnutrition in preoperative patients may be much higher than described before surgery (36), especially in weak and elderly patients. These patients often only have decreased appetite, insufficient food absorption, conversion and utilization, fatigue, mild abnormal blood indicators, which are high risks of malnutrition without showing significant weight loss, so the doctor in charge may offer them nutritional support. Our study found that patients in the PN group were older and had a lower muscle mass, lower hemoglobin and albumin levels, and a later tumor stage, which made patients more susceptible to malnutrition; moreover, the PN group had shorter survival time (P=0.023). In the analysis of risk factors for postoperative complications, we found that advanced age (≥70 years old), CCI 2–6 points, and open surgery and Roux-en-Y anastomosis of the digestive tract increase the probability of postoperative complications, which may be due to the increase of operation complexity, prolonged operation time, greater trauma to the human body, and stronger stress response. However, the factors mentioned above often cannot be changed, increasing the difficulty of clinical intervention. Cox regression analysis of survival showed that age ≥70 years, Roux-en-Y anastomosis, combined organ excision, low differentiation, and high TNM stage were independent risk factors for reducing postoperative survival, which was similar to our previous finding (37). PN did not affect long-term survival (P=0.950) regardless of whether patients were grouped according to SMI, TNM stage, or tumor differentiation. Huang *et al.* and Xu *et al.* demonstrated that short-term preoperative PN (3–7 days) did not significantly improve the prognosis of patients with GC at high risk of malnutrition or sarcopenia (21,22), which is similar to our results. We also found no significant effect of short-term preoperative PN on long-term survival (P=0.950). One possible reason for this is that the physiological functions of the human body do not recover within the first 7 days after PN. Due to the short duration of preoperative nutritional support, nutritional reserves may be insufficient for supporting protein synthesis, immune response, and acute wound healing (11). The patients most likely to benefit from preoperative PN are those least likely to tolerate oral administration and/or EN. However, we excluded patients who had to fast due to bleeding, perforation, or acute obstruction and those who were in urgent need of PN, thereby reducing the effect of PN.

Malnutrition is closely related to sarcopenia, and they share many pathophysiological components (38-40). Sarcopenia has been recognized as an independent risk factor for postoperative complications and may increase the risk of total and major complications after GI tumor resection by approximately 30% to 40% (27,41-43). This study did not find muscle mass or high risk of malnutrition to be independent risk factors for postoperative complications. Since this study was conducted in China, most patients with GC underwent preoperative CT scans, and CT is considered one of the gold standards for measuring muscle mass (44). The 19.3% prevalence of low muscle mass and 29.6% prevalence of high risk of malnutrition in our study are somewhat lower than those in our previous reports (22,27). This may be due to the fact that we excluded patients who received PN for at least 7 days before surgery, and these patients might have a higher probability of reduced muscle mass and a higher risk of malnutrition. In addition, muscle function indicators such as strength and gait speed, which may reduce the impact of sarcopenia on prognosis, were not included in this study. Subgroup analysis showed that PN support did not effectively improve the short-term prognosis of various patients after surgery. However, it may be beneficial in patients with albumin levels <35 g/L, open surgery, Roux-en-Y anastomosis, or TNM stage III, but there was no statistically significant difference. Amino acid preparations are important components of intravenous nutritional supplement that promote protein synthesis in the body. A higher serum albumin level may be a protective factor for improved surgical complications and survival (45). Further analysis is needed to determine whether long-term PN is beneficial to the prognosis of these patients.

Many factors known to influence clinical outcomes, such as age, diabetes, and other chronic diseases, cannot or are difficult to change preoperatively, and nutritional support is easily modifiable by the surgeon. For patients undergoing GI cancer surgery, improved physiological reserve means greater adaptability and resilience to surgical stress. However, PN seems to be used inappropriately in many elective abdominal procedures. We found that in patients who could tolerate oral feeding, clinical results were not significantly improved by preoperative short-term PN, and in the absence of clinical benefit, PN increased the economic burden of patients (post-PSM: ¥55,953.1 *vs.* ¥59,709.6, P<0.001), which is contrary to the principle of efficient health care resource utilization. Therefore, it is important for clinicians to solidly grasp the indications of preoperative nutritional therapy, and short-term PN support should not be the first choice.

Our study also had some limitations. First, only two centers and a limited number of patients were employed in the study. Second, PSM only controlled for the effects of measurable variables and to some extent the effects of confounding factors, but there were still some unmeasured confounders that could have introduced bias. In addition, PSM reduced the sample size, which changed the characteristics of the population to a certain extent and decreased the representativeness of the sample. Therefore, multicenter, prospective, randomized trials are urgently needed to confirm our conclusions.

Conclusions

Short-term preoperative PN does not improve postoperative clinical outcomes in patients with GC and may even increase the economic burden. PN is not recommended for patients who can tolerate oral feeding, and a firmer understanding of the indications and duration of preoperative nutritional support is needed.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://jgo.amegroups.com/article/view/10.21037/jgo-23-1000/rc

Data Sharing Statement: Available at https://jgo.amegroups.com/article/view/10.21037/jgo-23-1000/dss

Peer Review File: Available at https://jgo.amegroups.com/article/view/10.21037/jgo-23-1000/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jgo.amegroups.com/article/view/10.21037/jgo-23-1000/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the ethics committee of the First Affiliated Hospital of Wenzhou Medical University (No. KY2022-202) and the Second Affiliated Hospital of Wenzhou Medical University was informed and agreed to this study. Individual consent for this retrospective analysis was waived.

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