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Original Article

Insufficient enteral nutrition is an independent risk factor for poor clinical outcomes in gastric cancer patients following radical gastrectomy

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Abstract: Objective: To investigate the factors influencing inadequate enteral nutrition (EN) after radical gastrectomy for gastric cancer and its impact on clinical outcomes. Methods: A retrospective analysis was conducted on 212 gastric cancer patients who underwent radical surgery and received EN at the Fourth Hospital of Hebei Medical University. Patients were divided into two groups based on whether they achieved 60% of their caloric needs by the sixth postoperative day. Univariate and multivariate logistic regression models were used to identify factors associated with inadequate EN. Results: Inadequate EN was observed in 26.89% of the patients. Key factors associated with insufficient EN included delayed initiation of nutrition, increased intra-abdominal and central venous pressures, use of sedatives, and delayed early mobility (all $P<0.05$). Patients with inadequate EN had longer hospital stays, delayed bowel recovery, higher postoperative complication rates, and lower overall and disease-free survival rates (all $P<0.05$). Conclusion: Inadequate enteral nutrition is an independent risk factor for poor clinical outcomes in gastric cancer patients after radical gastrectomy. Early and adequate nutritional support is essential to improve recovery and long-term survival.

Keywords: Gastric cancer, enteral nutrition, malnutrition, influencing factors

Introduction

Gastric cancer (GC) is the fifth most common cancer and the third leading cause of cancer-related death worldwide, seriously threatening human life and health. According to the latest statistics, despite the decline in incidence, gastric cancer remains a major health problem worldwide. East Asia has the highest age-standardized incidence rate (ASR) of GC, followed by Central and Eastern Europe and South America [1, 2]. In addition to *Helicobacter pylori* infection, the occurrence of gastric cancer is also related to genetic risk factors and lifestyle factors such as drinking, smoking and high-salt diet [3]. Currently, radical treatment of gastric cancer mainly includes complete surgical resection, supplemented by neoadjuvant or adjuvant chemotherapy, with or without radiotherapy, to improve patient survival [4]. For most patients undergoing gastric cancer surgery, early postoperative enteral nutrition (EN) is generally safe and can improve short-term outcomes. However, the perioperative EN process requires dynamic evaluation to identify any potential contraindications. In cases of absolute contraindications, such as complete intestinal obstruction, uncontrollable peritonitis, intestinal ischemia, or severe shock, total parenteral nutrition should be given promptly [5]. Due to factors such as tumor's high metabolic state before surgery, the stress of surgical trauma, and postoperative dietary challenges or complications, gastric cancer patients often experience varying degrees of malnutrition, which seriously affects the patient's postoperative recovery [6].

Enteral nutrition is widely used clinically due to its safety, affordability, and ability to meet human physiological needs [7], particularly by supporting protein synthesis and metabolism. Current expert research consensus emphasizes the importance of early enteral nutrition support for improving patients' physical condition and surgical prognosis [8]. The European Society for Parenteral and Enteral Nutrition (ESPEN) clinical practice guidelines recommend

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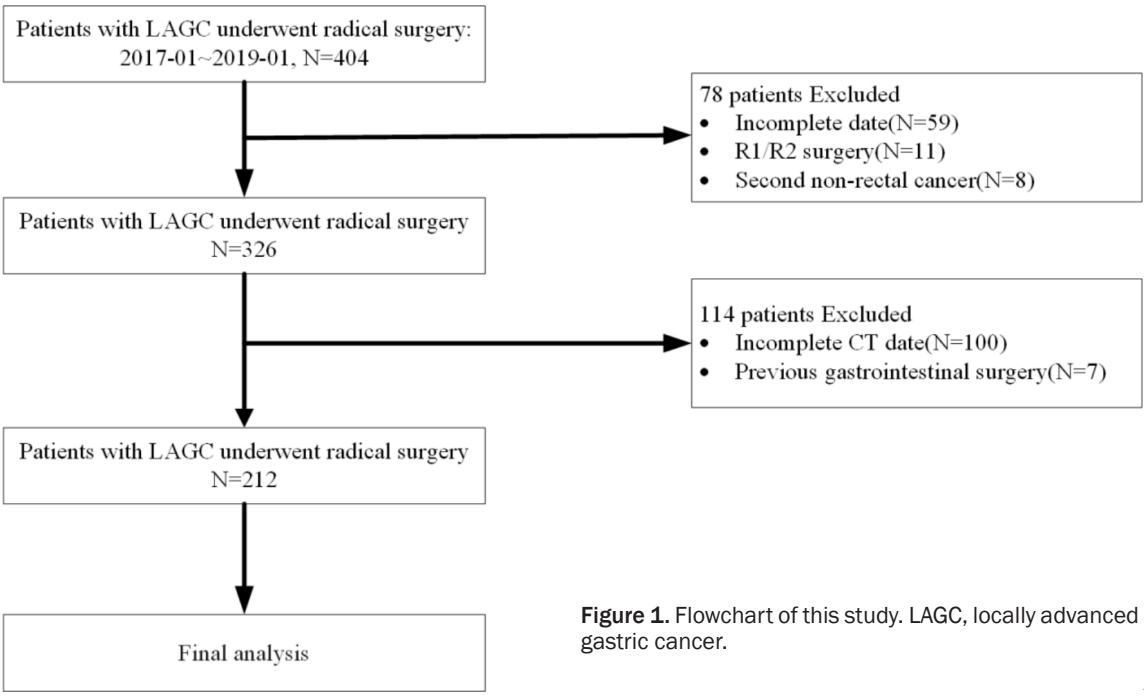

Figure 1. Flowchart of this study. LAGC, locally advanced gastric cancer.

initiating enteral nutrition within 24 hours after surgery for patients with gastrointestinal tumors, with an energy requirement of 25 to 30 kcal/kg/day. Achieving 50-65% of target energy requirements through enteral nutrition within the first week has been shown to yield significant clinical benefits [6, 9]. Similarly, enteral nutritional support is also critical for enhanced recovery after surgery, with recommendations suggesting a minimum of 30 kcal/kg/day to meet the body's needs [10].

However, most patients have insufficient energy intake, i.e., insufficient feeding, during enteral nutrition following gastric cancer surgery, with an incidence as high as 79.27% [11]. Patients' inability to obtain adequate energy and nutrition may lead to adverse clinical outcomes, such as infection, pressure sores, slow wound healing, and prolonged hospitalization [12]. Therefore, reasonable, adequate, and effective enteral nutrition support is extremely important for accelerating the recovery of gastric cancer patients after surgery. This study aims to explore the influencing factors for inadequate enteral nutrition after radical resection of gastric cancer and assess its impact on clinical prognosis, offering guidance for individualized precision treatment and nursing plans for patients with inadequate enteral nutrition.

Materials and methods

Case selection

A retrospective analysis was conducted on patients who underwent radical gastric cancer surgery and required enteral nutrition in the Third Department of Surgery, the Fourth Hospital of Hebei Medical University, from January 2017 to January 2019.

Inclusion criteria: Preoperative gastroscopy biopsy confirmed adenocarcinoma; Preoperative imaging showed no distant metastasis; Sufficient organ function to tolerate radical gastric cancer surgery; Adequate preoperative intestinal function for enteral nutrition; complete clinicaldata. Exclusion criteria: distant metastasis confirmed by preoperative imaging; Hemodynamic instability requiring continuous fluid resuscitation, significant acidosis (pH<7.25), and gastrointestinal perforation, or other enteral feeding contraindications; discontinuation of enteral nutrition due to other factors. According to the above inclusion and exclusion criteria, a total of 212 patients were included. The flow chart of patient inclusion is shown in **Figure 1**.

This study was approved by the hospital's ethics committee with ethics number of 2020-KY109. This study complies with the principles

of the Declaration of Helsinki and relevant ethical requirements.

Nutritional support method

All patients had a nasogastric tube placed during surgery, and postoperative sequential nutritional support was initiated. Parenteral nutrition was given on the day of surgery, and enteral nutrition support was started 24 hours after surgery, with preparations adjusted according to the recovery of the patient's intestinal function. The principle of "increasing concentration from low to high, volume from small to large, and speed from slow to fast" was followed. The 212 included patients were divided into enteral nutrition completion group (n=155) and non-completion group (n=57), based on whether the calorie intake from enteral nutrition preparations by the 6th day reached 60% of the patient's requirement (104.6 kJ or 25 kcal/kg/day) [8-10]. This classification was used to analyze the factors contributing to non-compliance within an enteral nutrition regimen.

Observation indicators

Primary observation outcomes: The surgery related indicators (type of surgery performed, operation time, intraoperative blood loss, and use of sedative), tumor stage, enteral nutrition implementation time, serum albumin level before enteral nutrition treatment, acute physiology and chronic health score (APACHE II; encompassing acute physiology score, age score, and chronic health score; the total score ranges from 0 to 71, with higher scores indicating a greater risk of in-hospital death), dietary fiber addition, intra-abdominal pressure (bladder pressure measurement, gastric pressure measurement, rectal pressure measurement, and inferior vena cava pressure measurement. Bladder pressure measurement is usually used to reflect intra-abdominal pressure), central venous pressure (by connecting an infusion set to a central venous catheter, draining the fluid, and measuring the height of the liquid column, with normal values ranging from 5 to 12 cm) and postoperative mobilization on the first postoperative day (time to first out-of-bed activity) were recorded and compared between the two groups.

Secondary observation outcomes: General patient information, including sex age, weight, and nutritional risk screening score (NRS 2002) were collected and compared between the two groups. Factors leading to insufficient enteral nutrition, such as unplanned extubation (where the patient removes the nasogastric tube without medical consent, or the tube falls out due to improper handling by medical staff, potentially affecting postoperative recovery) were documented. The actual enteral nutrition intake from the 1st to 5th day after surgery was calculated.

Statistical analysis

SPSS 21.0 statistical software was used to process the data. Measurement data were expressed as mean ± SD, and independent sample t-test was used for analysis. Count data were expressed as rate or percentage, and chi-square test was adopted for analysis. Univariate and multivariate logistic regression analyses were used to identify independent risk factors for incomplete enteral nutrition as well as the independent prognostic factors for gastric cancer patients. $P<0.05$ was considered statistically significant.

Results

Clinical and pathological characteristics of patients

A total of 57 patients (26.89%) failed to complete the enteral nutrition. Among them, 10 patients (17.54%) had unplanned extubation, and 47 patients (82.46%) had enteral nutrition intolerance (abdominal distension in 28 cases, nausea and vomiting in 23 cases, diarrhea in 11 cases, constipation in 5 cases, diarrhea and abdominal distension in 10 cases, abdominal distension with nausea and vomiting in 7 cases, and alternating abdominal distension, diarrhea and constipation in 3 cases). The age of the patients in the completion group ranged from 52 to 78 years old, with an average age of (63.14 ± 6.39) years old, including 104 male and 51 female patients; the age of the patients in the non-completion group ranged from 50 to 79 years old, with an average age of (62.20 ± 6.57) years old, including 37 male and 20 female patients. The clinical data of the two groups of patients were similar in gender, age, weight, body mass index (BMI), ASA anesthesia grade, NRS2002 score, serum albumin (all

Table 1. Comparison of baseline clinical and pathological characteristics between the two groups

	Completion group (N=155)	Non-completion Group (N=57)	*P*-value
Gender			0.765
Male	104	37	
Female	51	20	
Age (years)	6 3 ± 6.4	6 20 ± 6.6	0.541
Weight (kg)	57.42 ± 11.21	60.21 ± 9.65	0.582
BMI (kg/m^2, x ± s)	22.31 ± 3.64	22.83 ± 3.81	0.631
ASA anesthesia grade (points)	2.11 ± 1.34	1.97 ± 0.87	0.734
NRS2002 score (points)	3.56 ± 1.12	3.24 ± 1.54	0.660
Serum albumin (g/L)			0.066
≤25	65	32	
>25	90	25	
Tumor stage			0.549
I	53	17	
II/III	102	40	
Surgical approach			0.041
Laparotomy	60	31	
Laparoscopy	95	26	
Operation time (min)	198.30 ± 22.55	202.65 ± 23.41	0.087
Intraoperative blood loss (ml)	204.32 ± 80.88	214.04 ± 57.60	1.115
Acute Physiology and Chronic Health Score (points)			<0.001
<20	100	15	
≥20	55	42	
Timing of enteral nutrition initiation (h)			<0.001
24 hours after surgery	74	9	
48 hours after surgery	81	48	
Intra-abdominal pressure (mmhg)			<0.001
≤15	100	18	
>15	55	39	
Central venous pressure (cmH_2O)			<0.001
≤10	88	17	
>10	67	40	
Sedative use			0.042
Yes	100	28	
No	55	29	
Dietary fiber supplementation			0.014
Yes	81	19	
No	74	38	
Time to ambulation on the first day after surgery (h)			0.047
≥4	80	20	
<4	75	37	

Note: BMI, body mass index. Tumor staging: early stage is AJCC-Stage TNM stage I-II, and middle and late stage is stage III-IV.

P>0.05). The statistical results showed that the patients who did not complete the nutritional therapy had significantly higher acute physiological and chronic health scores, delayed enteral nutrition initiation, higher intra-abdominal pressure and central venous pressure, sedative use, dietary fiber supplementation, and delayed time to ambulate on the first day after surgery than those who completed the nutritional therapy (all *P*<0.05) (**Table 1**).

Table 2. Univariate analysis of factors contributing to unfinished EN after radical surgery in GC patients

Clinical factors	OR	95% CI	*P*-value
Gender (male *vs.* female)	0.562	0.212-1.432	0.405
Age (≤60 *vs.* >60)	0.894	0.434-1.804	0.743
BMI (kg/m^2, x ± s)	0.743	0.402-1.739	0.188
ASA anesthesia classification (points)	0.690	0.389-1.134	0.423
NRS2002 score (points)	0.795	0.532-1.923	0.089
Serum albumin (g/L) (≤25 *vs.* >25)	0.873	0.474-1.983	0.783
Tumor stage (early *vs.* Progressive stage)	1.234	0.982-2.314	0.067
Surgical method (laparoscopic *vs.* laparotomy)	0.388	0.054-0.982	0.022
Operation time (min)	0.892	0.254-1.245	0.457
Intraoperative blood loss (ml)	0.674	0.241-1.165	0.085
Acute Physiology and Chronic Health Score (<20 *vs.* ≥20)	0.482	0.231-0.873	0.003
Enteral nutrition start time (h) (≤48 *vs.* >48)	2.314	1.309-4.893	<0.001
Intra-abdominal pressure (mmHg) (≤15 vs. >15)	1.567	1.023-2.483	0.011
Central venous pressure (cmH_2O) (≤10 vs. >10)	1.490	1.004-2.348	0.029
Sedative use (yes *vs. No*)	0.634	0.312-0.982	0.004
Dietary fiber supplementation (yes *vs. No*)	0.482	0.143-0.723	0.003
Time to ambulation on the first day after surgery (h) (≥4 *vs.* <4)	1.430	1.023-1.998	0.031

Univariate analysis of factors associated with incomplete EN in patients with gastric cancer after radical resection

Univariate analysis showed that surgical method, APACHE II score, timing of enteral nutrition initiation, intra-abdominal pressure, central venous pressure, sedative use, dietary fiber supplementation, and time to ambulation on the first post-operative day were closely associated with incomplete enteral nutrition in gastric cancer patients (all *P*<0.05), while age, sex, BMI, operation time, ASA anesthesia grade, NRS-2002 score, serum albumin, tumor stage, operation time, and intraoperative blood loss were not (all *P*>0.05) (**Table 2**).

Multifactor analysis of uncompleted EN in patients with gastric cancer after radical resection

The variables with statistical significance in the univariate analysis were included in the logistic regression analysis. The results showed that APACHE II scores, timing of enteral nutrition initiation, intra-abdominal pressure, central venous pressure and time to ambulation on the first postoperative day were the independent risk factors for incomplete EN in patients with gastric cancer after radical resection (**Table 3**).

Impact of incomplete EN on the short-term clinical outcomes of patients with gastric cancer

A total of 53 patients (25.00%) developed postoperative complications, including 33 (62.26%) in the non-completion group and 20 (37.74%) in the completion group (P=0.028). Additionally, patients in the completion group experienced shorter postoperative flatulence and defecation times, as well as shorter hospital stays, compared to those in the non-completion group (all *P*<0.001) (**Table 4**).

Effect of incomplete EN after radical resection on the long-term clinical outcomes of patients with gastric cancer

By the end of the follow-up period, 32 patients (15.1%) were lost to follow-up, with a median follow-up time of 57.8 months. Among the 180 patients with complete follow-up information, 47 (26.1%) were from the non-completion group and 133 (73.9%) were from the completion group. Besides, 88 patients (48.9%) died during the follow-up period. Among the 47 patients in the non-completion group, 35 patients (74.5%) died, with a 5-year overall survival rate of 25.5% (12/47) and a 5-year disease-free survival rate of 21.3% (10/47); among the 133 patients in the completion

Table 3. Multivariate analysis of independent factors contributing to incomplete EN in patients with gastric cancer following radical resection

Clinical factors	β	SE	OR	95% CI	*P*-value
Surgical method (*laparoscopic vs. laparotomy*)	0.703	0.399	1.108	0.227-2.082	0.078
Acute Physiology and Chronic Health Score (<20 *vs.* ≥20)	0.259	0.402	0.423	0.129-0.625	0.002
Enteral nutrition start time (h) (≤48 *vs.* >48)	1.716	0.467	0.220	0.072-0.449	<0.001
Intra-abdominal pressure (mmHg) (≤15 vs. >15)	1.427	0.407	0.327	0.108-0.532	<0.001
Central venous pressure (cmH_2O) (≤10 vs. >10)	1.39 1	0.423	0.242	0.109-0.569	0.001
Sedative use (yes *vs. No*)	0.769	0. 404	1.620	0.210-2.023	0.057
Dietary fiber supplementation (yes *vs. No*)	0.619	0.403	0.658	0.244-1.187	0.125
Time to ambulation on the first day after surgery (h) (≥4 *vs.* <4)	1.092	0.420	2.767	1.563-5.712	0.009

Table 4. The impact of incomplete EN on postoperative gastric cancer patients

Influencing factors	Completion group (N=155)	Non-completion Group (N=57)	Measurement value	*P*-value
Postoperative flatus time (h)	59.17 ± 9.91	69.42 ± 9.75	-6.148	<0.001
Postoperative defecation time (h)	77.75 ± 8.61	84.07 ± 9.28	-4.463	<0.001
Postoperative hospital stay (h)	12.14 ± 2.89	16.77 ± 3.66	-8.630	<0.001
Wound infection (%)	13 (8.39)	7 (12.28)	0.234	0.390
Fat liquefaction (%)	16 (10.32)	9 (15.79)	1.197	0.274
Intestinal obstruction (%)	8 (5.16)	5 (8.77)	0.421	0.517
Anastomotic leakage (%)	4 (2.58)	3 (5.26)	0.287	0.592
Total complications	33 (15.57)	20 (35.09)	4.231	0.040

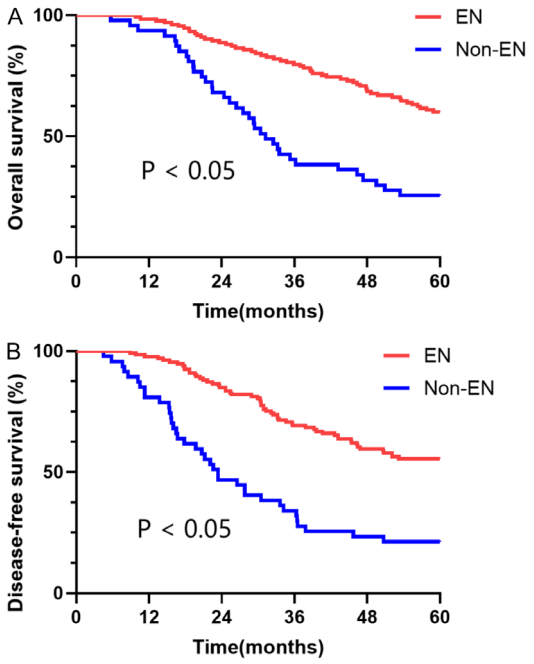

Figure 2. Survival analysis of enrolled patients. A. 5-year overall survival analysis; B. 5-year disease-free survival analysis.

group, 53 patients (39.8%) died, with a 5-year overall survival rate of 60.2% (80/133) and a 5-year disease-free survival rate of 56.4% (75/133). The 5-year overall survival rate and disease-free survival rate of the non-completion group were significantly lower than those of the completion group (all P<0.05) (**Figure 2**). Further Cox multivariate analysis showed that timely initiation of enteral nutrition after radical surgery was an independent risk factor affecting the 5-year overall survival rate and disease-free survival rate in gastric cancer patients (**Table 5**).

Discussion

In recent years, the concept of enhanced recovery after surgery (ERAS) has gradually been applied to the field of gastric surgery. Nutritional management, as an important component of the concept of ERAS, is an interdisciplinary challenge aimed at reducing perioperative stress and improving clinical outcomes. Early enteral nutrition after surgery can maintain normal intestinal barrier function, moderately stimulate immune response, and reduce intestinal flora displacement [13, 14]. Studies have shown that malnutrition is associated with poor prognosis in surgical patients. A meta-analysis of 29 studies (involving 7,179 patients)

Table 5. Multivariate analysis of the factors for the prognosis of gastric cancer patients

Independent factor	5-year OS Multivariate analysis			5-year DFS Multivariate analysis		
	HR	95% CI	*P* value	HR	95% CI	*P* value
Age (years)			0.333			0.209
<60	1.000	reference		1.000	reference	
≥60	1.435	0.672-1.992		0.983	0.632-1.634	
Tumor size (cm)			0.609			0.324
<5.0	1.000	reference		1.000	reference	
≥5.0	1.098	0.763-2.094		1.409	0.923-1.894	
Differentiation			0.002			0.003
Poor	1.000	reference		1.000	reference	
Moderately or well	2.109	1.378-4.893		2.248	1.702-5.233	
TNM stage			<0.001			<0.001
I and II	1.000	reference		1.000	reference	
III	4.988	2.311-9.982		4.672	2.109-7.233	
Chemotherapy			<0.001			<0.001
Yes	1.000	reference		1.000	reference	
No	3.234	1.204-6.242		2.802	1.230-4.781	
EN			<0.001			<0.001
Yes	1.000	reference		1.000	reference	
No	2.394	1.389-5.999		2.092	1.634-4.902	

Note: SII, Systemic immune-inflammatory index; PNI, prognostic nutritional index; EN, enteral nutrition.

revealed that postoperative sarcopenia in patients with gastrointestinal tumors was associated with an increased risk of major and overall postoperative complications [15, 16]. Therefore, perioperative nutritional support is essential for patients with malnutrition and nutritional risks.

In 2021, the European Society of Clinical Nutrition and Metabolism (ESPEN) [11] issued guidelines for clinical nutrition in surgery. For patients who cannot eat for more than 5 days during the perioperative period, or whose oral intake fails to maintain more than 50% of the recommended intake, an enteral nutrition support should be initiated immediately [17-19].

A Meta-analysis conducted on 29 trials confirmed that enteral nutrition can significantly reduce the incidence of infectious complications and anastomotic leaks in patients after gastrointestinal surgery; another Meta-analysis based on 18 randomized controlled trials showed that enteral nutritional supplements could shorten the time to flatulence, reduce hospital stay, and increase albumin levels. Kudsk et al. found that early enteral nutrition can reduce the incidence of postoperative complications and multi-organ failure [20-24]. In our study, patients in the enteral nutrition completion group had significantly shorter postoperative flatus, defecation time, and hospital stay; in addition, our results showed that compared with the completion group, patients who did not complete enteral nutrition were more likely to develop related complications.

Enteral nutrition support for postoperative gastrointestinal tumor patients not only provides essential calories and nutrients but also improves the intestinal mucosal barrier function and promotes gastrointestinal motility and wound healing [25]. However, in clinical practice, enteral nutrition is often administered at low doses, leading to a high incidence of inadequate feeding. In this study, only 73.11% (155/212) of gastric cancer patients following radical surgery achieved the target enteral nutrition amount. Factors contributing to inadequate feeding include unplanned extubation, enteral nutrition intolerance (e.g., abdominal issues, diarrhea, nausea, vomiting), postoperative complications affecting gastrointestinal function (e.g., anastomotic obstruction, gastric emptying issues), and insufficient intake or absorption of enteral nutrition for at least one week [26]. Incorrect nutritional formulas and improper feeding methods can exacerbate en-

teral nutrition intolerance, impeding infusion rate and leading to inadequate feeding. A study by Weng et al. reported a 68% incidence of enteral feeding intolerance, manifesting as abdominal pain, bloating, nausea, and vomiting [27]. Yao et al. analyzed the risk factors for inadequate enteral nutrition in 27 ICU patients and found that the main factors for inadequate enteral nutrition in patients were abdominal distension (33.33%), gastric retention (18.52%), and vomiting (11.11%) [28]. In addition, the energy demand of gastric cancer patients after surgery is also affected by the patient's weight and intraoperative blood loss [11, 29, 30]. Among patients with unplanned extubation, most exhibited intolerance to enteral nutrition, with symptoms including abdominal distension (28 cases), nausea and vomiting (23 cases), diarrhea (11 cases), and constipation (5 cases). Independent factors contributing to inadequate enteral nutrition after radical gastric cancer resection include APACHE II score, delayed initiation of enteral nutrition, elevated intra-abdominal pressure, central venous pressure, and delayed early postoperative mobilization. Critically ill patients, those with major trauma, and individuals requiring enteral nutrition to meet their energy needs often experience low adherence to enteral nutrition due to intolerance. Patient cooperation, nursing practices, and physician management significantly impact the success of enteral nutrition. Future studies should comprehensively analyze these factors to improve outcomes. In the incomplete enteral nutrition group, complications, intolerance, incomplete obstruction, and unplanned extubation posed significant challenges to successful enteral nutrition completion. Further research should focus on these issues to develop more effective strategies for managing enteral nutrition in postoperative gastric cancer patients.

A prospective randomized study on early enteral nutrition after gastric cancer surgery by Marano et al. showed that early enteral nutrition after surgery significantly reduced postoperative infectious complications, shortened hospital stay, and improved anastomotic healing [31]. However, individualized enteral nutrition dosing based on patient weight was rarely implemented, potentially causing inadequate feeding. To address this, larger-scale, prospective, randomized, double-blind studies are necessary. Zhang et al. enhanced standardized enteral nutrition implementation through multidisciplinary collaboration, creating an optimal nutrition support plan [6]. Inadequate enteral nutrition support often arises from failing to meet target nutritional needs. The American Society for Parenteral and Enteral Nutrition (ASPEN) suggests setting initial goals, conducting ongoing evaluation, and gradually increasing feeding to enhance enteral nutrition adaptation [32]. Physicians should determine enteral nutrition dosage based on patient-specific factors such as weight, blood loss, and tolerance. Nurses play a critical role by educating patients on the importance of enteral nutrition, following established protocols, monitoring tolerance, and adjusting intake promptly. Moreover, patients and families should understand the benefits of enteral nutrition, cooperate with treatment plan, and report any discomfort promptly.

While this study identified important factors like surgical method and the timing of enteral nutrition initiation, other key factors such as intolerance to nutritional preparations, incomplete obstruction, and unplanned extubation were not thoroughly investigated due to the retrospective nature of the study. These gaps will be addressed in future research to provide a more comprehensive understanding of the factors influencing enteral nutrition outcomes.

This study identified factors influencing inadequate enteral nutrition after radical gastrectomy and its association with delayed recovery, increased complications, and lower survival rates. Key factors include the timing of EN initiation, intra-abdominal and central venous pressures, and sedative use. However, given the study's retrospective design and reliance on single-center data, further prospective, multicenter studies are needed to validate these findings. Future research should focus on developing standardized protocols for early and adequate nutritional support to improve clinical outcomes in gastric cancer patients.

Acknowledgements

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Disclosure of conflict of interest

None.

Abbreviations

ASR, age-standardized incidence rate; ESPEN, the European Society for Parenteral and Enteral Nutrition; NRS, nutritional risk screening; EEN, early enteral nutrition; TPN, total parenteral nutrition; SII, systemic immune-inflammatory index; LAGC, locally advanced gastric cancer; PNI, prognostic nutritional index.

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