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ABOUT COVER

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ORIGINAL ARTICLE

Retrospective Study

Clinical significance of preoperative nutritional status in elderly gastric cancer patients undergoing radical gastrectomy: A single-center retrospective study

Xi-Ning Zhao, Jing Lu, Hong-Yong He, Sheng-Jin Ge

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Abstract

BACKGROUND

The population of elderly patients with gastric cancer is increasing, which is a major public health issue in China. Malnutrition is one of the greatest risk factors for adverse clinical outcomes in elderly patients with gastric cancer.

AIM

To investigate the preoperative nutritional status and its association with delayed discharge of elderly gastric cancer patients following radical gastrectomy.

METHODS

A total of 783 patients aged 65 years and older harboring gastric adenocarcinoma and following radical gastrectomy were retrospectively analyzed from the prospectively collected database of Zhongshan Hospital of Fudan University between January 2018 and May 2020.

RESULTS

The overall rate of malnutrition was 31.8%. The incidence of postoperative complications was significantly higher in the malnourished group compared to the well-nourished group ($P < 0.001$). Nutritional characteristics in the malnou-

rished group, including body mass index, prognostic nutritional index (PNI), albumin, prealbumin, and hemoglobin, were all significantly lower than those in the well-nourished group. The percentage of patients who received postoperative total nutrient admixture was lower in the malnourished group compared to the well-nourished group (22.1% *vs* 33.5%, $P = 0.001$). Age ≥ 70 years (HR = 1.216, 95%CI: 1.048-1.411), PNI < 44.5 (HR = 1.792, 95%CI: 1.058-3.032), operation time ≥ 160 minutes (HR = 1.431, 95%CI: 1.237-1.656), and postoperative complications grade III or higher (HR = 2.191, 95%CI: 1.604-2.991) were all recognized as independent risk factors associated with delayed discharge.

CONCLUSION

Malnutrition is relatively common in elderly patients undergoing gastrectomy. Low PNI is an independent risk factor associated with delay discharge. More strategies are needed to improve the clinical outcome of these patients.

Key Words: Gastric cancer; Preoperative nutritional status; Malnutrition; Elderly; Radical gastrectomy

Core Tip: Malnutrition is a significant risk factor for adverse clinical outcomes in elderly gastric cancer patients. In our investigation of the nutritional status and perioperative nutritional support of elderly surgical patients with gastric cancer, we discovered that the overall frequency of malnutrition was 31.8%. The incidence of postoperative complications in the malnourished group was significantly higher than that in the well-nourished group. Nutritional characteristics of patients in the malnourished group were recognized as independent risk factors associated with delayed discharge.

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INTRODUCTION

Gastric cancer remains the fifth most common malignant cancer and the fourth leading cause of cancer-related mortality [1,2]. Due to economic development and increased life expectancy, the population of elderly patients with gastric cancer is increasing, which is a major public health issue in China[3]. Currently, radical gastrectomy is recognized as the standard treatment for managing resectable gastric cancer[4]. Elderly patients with gastric cancer encounter numerous treatment challenges, including immunosuppression, comorbidities, organ dysfunction, and delayed recovery[5]. Advanced age is linked to a higher incidence of postoperative complications shortly after surgery and lower 5-year overall survival rate as long-term outcomes[6,7].

In China, the prevalence of malnutrition among hospitalized patients ranges from approximately 12.6% to 46.19%[8]. Malnutrition is a significant risk factor for adverse clinical outcomes in elderly gastric cancer patients[9]. At the time of diagnosis, nutritional status is independently linked to postoperative complications, disease-free survival, and overall survival[10,11]. This condition may arise from mechanical partial or complete obstruction of the digestive tract and cancer anorexia-cachexia syndrome, resulting in insufficient intake of energy or protein and disorders of absorption. Effective nutritional management involves three key steps: Screening, assessment, and intervention.

Most previous studies have concentrated on hospitalized internal medical patients[12], with only a few addressing surgical patients regardless of age[13]. Thus, in this retrospective study, we aim to investigate the nutritional status and perioperative nutritional support of elderly surgical gastric cancer patients, providing a basis for implementing effective nutritional interventions.

MATERIALS AND METHODS

Study design and patients

We prospectively recruited consecutive patients with gastric cancer, collected their clinicopathological data, and retrospectively analyzed their clinicopathological features. The records of elderly gastric cancer patients aged 65 years and older who underwent radical surgical resection of gastric adenocarcinoma between January 2018 and May 2010 were retrospectively identified, based on the database of patients with gastric cancer in the Department of General Surgery of Zhongshan Hospital of Fudan University (Shanghai, China). Patients with other malignancies, emergency surgery, previous gastrointestinal surgery, and incomplete clinical or pathological records were excluded. As a result, a total of 783 patients were included in the final analysis (Figure 1). A retrospective review of prospectively collected data was

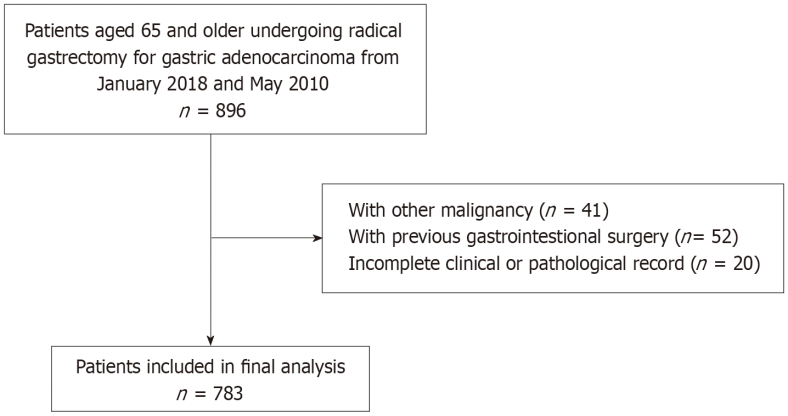

Figure 1 Flowchart of the inclusion process of patients.

performed, and the clinicopathological features, including demographic information, medical history, laboratory tests, postoperative complications, length of stay (LOS), and cost of hospitalization, were collected and analyzed. The variables which reflected the nutritional status including albumin, prealbumin, hemoglobin, and total lymphocyte count were recorded from laboratory tests performed within one week prior to surgery. The cut-off value for albumin, prealbumin, and hemoglobin were defined using the lower limit of normal reference value of Zhongshan Hospital (albumin 30 g/L, prealbumin 180 mg/L, and hemoglobin 90 g/L). Clavien-Dindo complication grading criteria was used to grade surgical complications[14]. The research was conducted in accordance with the Declaration of Helsinki, and ethical approval (B2021-392) was granted by the Clinical Research Ethics Committee of Zhongshan Hospital of Fudan University (Shanghai, China). Signed informed consent was obtained from all patients for the acquisition and use of anonymized clinical data.

Definition and assessment of malnutrition

Malnutrition is a serious condition that occurs when the diet does not contain the right amount of nutrients. It means "poor nutrition" and can refer to undernutrition and overnutrition[15]. In this study, we focus on undernutrition in elderly gastric cancer patients. According to the European Society for Clinical Nutrition and Metabolism (ESPEN) diagnostic criteria, malnutrition is defined as unintentional weight loss of more than 5% over the last 3 months and a body mass index (BMI) less than 20 kg/m^2 for patients under 70 years old, or less than 22 kg/m^2 for those age 70 and older or more than 10% (regardless of time frame)[16]. Nutritional assessment is conducted using the prognostic nutritional index (PNI), a readily accessible tool widely used to evaluate the nutritional status of gastric cancer patients [17]. The PNI is calculated based on the following equation: [(0.005 × total lymphocyte count (/mm^3)) + (10 × serum albumin (g/dL))]. The cut-off value for PNI was defined using the median value. The composition and duration of nutritional management were recorded and analyzed.

Statistical analysis

Statistical analysis was performed with SPSS Software (version 25.0; SPSS Inc., Chicago, IL, United States). Normal distribution measurement data were expressed as mean ± SD, and t test was used to compare the differences between the groups. The measurement data of skewed distribution were expressed as median (interquartile range), and the categorical variables were expressed as counts and percentages and compared using the χ^2 test or Fisher's exact test. Univariate and multivariate analyses were conducted using the Cox proportional hazards regression model. Differences were considered statistically significant at values of $P < 0.05$.

RESULTS

General characteristics

Table 1 summarizes the clinical characteristics of elderly gastric cancer patients enrolled in this study, and their relationships with nutritional status. Most patients were male (74.6%) and the median age was 70 years at diagnosis, ranging from 65 to 86 years. 9.7% (76/783) of the patients suffered from 3 or more comorbidities, such as coronary heart disease, hypertension, chronic obstructive pulmonary disease, *etc.* Of these patients, 132 (16.9%) received preoperative consultation due to comorbidities. The overall frequency of malnutrition in the patients was 31.8% (249/783). The patients in the malnourished group were older than those in the well-nourished group ($P < 0.001$), and the incidence of postoperative complications in the malnourished group was significantly higher compared to that in the well-nourished group (grade I-II: 10.8% *vs* 6.9%; grade III and higher: 11.7% *vs* 4.0%; $P < 0.001$). While, the gender, comorbidity, anesthesia type, surgery type, operation time, preoperative consultation, neoadjuvant chemotherapy, TNM stage, cost of hospitalization, and unplanned readmission rate within 30 days were not statistically different between the two groups.

Table 1 Clinical characteristics of malnourished and well-nourished elderly patients

Factor	Malnourished		Well-nourished		*P* value	Total	
All patients	249	100	534	100		783	100
Age (years)					< 0.001		
Median (IQR)	72 (69, 76)		69 (67, 73)			70 (67, 74)	
Gender					0.762		
Female	65	26.1	134	25.1		199	25.4
Male	184	73.9	400	74.9		584	74.6
Comorbidity					0.321		
0-2	221	88.8	486	91.0		707	90.3
≥ 3	28	11.2	48	9.0		76	9.7
Type of anesthesia					0.073		
GA	35	14.1	52	9.7		87	11.1
TEA	214	85.9	482	90.3		696	88.9
Type of surgery					0.721		
Total gastrectomy	112	45.0	247	46.3		359	45.8
Distal gastrectomy	130	52.2	267	50.0		397	50.7
Proximal gastrectomy	7	2.8	20	3.7		27	3.5
Operation time (min)					0.082		
Median (IQR)	160 (126, 189)		160 (129, 191)			160 (123, 189)	
Preoperative consultation					0.303		
No	202	81.1	449	84.1		651	83.1
Yes	47	18.9	85	15.9		132	16.9
Neoadjuvant chemotherapy					0.647		
No	240	96.4	518	97.0		758	96.8
Yes	9	3.6	16	3.0		25	3.2
TNM stage					0.059		
I	32	12.9	87	16.3		126	16.1
II	53	21.3	133	24.9		150	19.2
III	164	65.8	314	58.8		507	64.7
Clavien-Dindo classification					< 0.001		
None	193	77.5	476	89.1		669	85.4
I + II	27	10.8	37	6.9		64	8.2
III or higher	29	11.7	21	4.0		50	6.4
Cost of hospitalization (× 10^3 RMB)					0.293		
Median (IQR)	55.3 (47.4, 66.6)		54.7 (47.8, 63.2)			54.8 (47.7, 64.7)	
Re-admission within 30 days	11	4.4	4	0.7	0.790	15	1.9

GA: General anesthesia; TEA: General anesthesia combined with thoracic epidural block; IQR: Interquartile range.

Perioperative nutritional characteristics

As shown in Table 2, nutritional characteristics of patients in the malnourished group, including BMI, PNI, albumin, prealbumin, and hemoglobin, were all significantly lower than those in the well-nourished group. However, the total lymphocyte count did not differ significantly between the two groups. To solve the problem of malnutrition in the 783 elderly gastric cancer patients enrolled in this study, 424 (54.1%) received preoperative nutritional support, and the

Table 2 Nutritional characteristics of malnourished and well-nourished elderly gastric cancer patients

Factor	Malnourished	Well-nourished	*P* value	Total
BMI (kg/m^2)	19.4 ±1.8	24.5 ± 2.6	< 0.001	22.9 ± 3.4
PNI	46.7 ± 5.7	48.8 ± 5.3	< 0.001	48.1 ± 5.6
Albumin (g/L)	39.1 ± 4.6	40.7 ± 4.0	< 0.001	40.2 ± 4.3
Prealbumin (mg/L)	193.2 ± 50.6	214.6 ± 47.7	< 0.001	207.8 ± 49.6
Hemoglobin (g/L)	117.0 ± 24.1	122.8 ± 23.1	0.001	121.0 ± 23.6
TLC (× 10^9/L)	1.57 ± 0.55	1.60 ± 0.54	0.472	1.59 ± 0.54

BMI: Body mass index; PNI: Prognostic nutritional index; TLC: Total lymphocyte count.

Table 3 Perioperative nutritional support among elderly gastric cancer patients

Factor	Malnourished		Well-nourished		*P* value	Total	
Preoperative nutrition					< 0.001		
Diet	141	56.6	218	40.8		359	45.9
Diet + single transfusion	77	30.8	295	55.4		373	47.6
TPN	31	12.4	20	3.7		51	6.5
Postoperative nutrition					0.001		
Single transfusion	194	77.9	355	66.5		549	70.1
TNA	55	22.1	179	33.5		234	29.9
Postoperative PN period (days)					0.951		
Median (IQR)	5 (4, 6)		5 (4, 6)			5 (4, 6)	
Postoperative EN period (days)					0.273		
Median (IQR)	2 (1, 3)		2 (1, 2)			2 (1, 2)	

EN: Enteral nutrition; PN: Parenteral nutrition; TPN: Total parenteral nutrition; TNA: Total nutrient admixture; IQR: Interquartile range.

nutritional support primarily consisted of carbohydrates derived from the diet. In the malnourished group, 30.8% (77/249) of the patients received a single nutritional transfusion and 12.4% (31/249) received total parenteral nutrition (TPN). In the well-nourished group, 55.4% (296/534) received a single nutritional transfusion and 3.7% (20/534) received TPN. The rate of preoperative TPN support was significantly higher in the malnourished group compared to the well-nourished group ($P < 0.001$) (Table 3).

After surgery, all patients received parenteral nutrition support. Among those in the well-nourished group, 77.9% (194/249) received a single transfusion of carbohydrates with or without composite amino acids, while 22.1% (55/249) received total nutrient admixture (TNA). In patients with normal nutritional status, 66.5% (355/534) of the patients received a single transfusion and 33.5% (179/534) of the patients received TNA. The proportion of patients who received TNA was notably lower in the well-nourished group compared to the malnourished group ($P = 0.001$). However, there were no significant differences in the postoperative nutritional support rates or duration between the two groups (Table 3).

Risk factors associated with prolonged LOS

The median LOS of elderly gastric cancer patients enrolled in this study was 8 days (Table 1). A LOS of 9 days or more was defined as prolonged LOS. In order to estimate the clinical factors that might influence the LOS, univariate analyses for LOS were performed. As shown in Table 4, clinical factors such as patient age, gender, nutritional status, postoperative nutritional support, operation time, anesthesia type, surgery type, postoperative complications, comorbidity, BMI, PNI, albumin, prealbumin, and hemoglobin were all included in the univariate analysis. Patient age, PNI, prealbumin, operation time, and comorbidities were significant predictors for prolonged LOS.

To evaluate the robustness of the value of significant predictors for prolonged LOS, Cox multivariate regression analyses were performed to derive risk estimates related to prolonged LOS with the same clinical parameters that showed significance in univariate analyses to control for confounders. As depicted in Table 5, age ≥ 70 years (OR = 1.216, 95%CI: 1.048-1.411, $P = 0.010$), PNI < 44.5 (OR = 1.792, 95%CI: 1.058-3.032, $P = 0.030$), operation time ≥ 160 min (OR = 1.431, 95%CI: 1.237-1.656, $P < 0.001$), and postoperative complications grade III or higher (OR = 2.191, 95%CI: 1.604-2.991, $P <$

Table 4 Univariate Cox regression analyses of clinical factors associated with length of stay

Factor	LOS (days)	Hazard ratio (95%CI)	*P* value
Age (years)[1]			0.002
< 70	7 (7, 9)	1.000 (reference)	
≥ 70	8 (7, 10)	1.620 (1.110-2.364)	
Gender			0.076
Female	7 (7, 9)	1.000 (reference)	
Male	8 (7, 10)	0.866 (0.568-1.319)	
Nutritional status			0.134
Well-nourished	8 (7, 9)	1.000 (reference)	
Malnourished	8 (7, 10)	0.652 (0.361-1.178)	
Operation time (min)[1]			< 0.001
< 160	7 (7, 8)	1.000 (reference)	
≥ 160	8 (7, 11)	2.307 (1.600-3.328)	
Type of anesthesia			0.099
GA	8 (7, 11)	1.000 (reference)	
TEA	8 (7, 9)	0.732 (0.432-1.238)	
Type of surgery			0.055
Distal gastrectomy	7 (7, 9)	1.000 (reference)	
Proximal gastrectomy	8 (7, 9)	0.611 (0.422-0.887)	
Total gastrectomy	8 (7, 10)	0.510 (0.173-1.500)	
Comorbidity			0.038
0-2	8 (7, 9)	1.000 (reference)	
≥ 3	8 (7, 11)	2.415 (1.819-3.411)	
BMI			0.088
≥ 20	8 (7, 10)	1.000 (reference)	
< 20	8 (7, 9)	0.565 (0.294-1.089)	
PNI[1]			0.005
≥ 44.5	8 (7, 11)	1.000 (reference)	
< 44.5	10 (7, 11)	3.940 (1.042-7.904)	
Albumin (g/L)			0.107
≥ 30	8 (7, 9)	1.000 (reference)	
< 30	9 (8, 13)	1.087 (0.734-1.610)	
Prealbumin (mg/L)			0.046
≥ 180	8 (7, 9)	1.000 (reference)	
< 180	8 (7, 10)	1.265 (1.133-1.919)	
Hemoglobin (g/L)			0.169
≥ 90	8 (7, 9)	1.000 (reference)	
< 90	8 (7, 11)	1.418 (0.852-2.360)	
Postoperative nutrition			0.337
Single transfusion	8 (7, 10)	1.000 (reference)	
TNA	8 (7, 9)	0.826 (0.558-1.221)	
Clavien-Dindo classification			< 0.001

None	8 (7, 9)	1.000 (reference)
I + II	10 (7, 12)	4.161 (2.199-7.876)
III or higher	10 (7, 17)	4.843 (2.771-8.464)

[1]Split at median.
LOS: Length of stay; GA: General anesthesia; TEA: General anesthesia combined with thoracic epidural block; BMI: Body mass index; PNI: Prognostic nutritional index; TNA: Total nutrient admixture.

Table 5 Multivariate Cox regression analyses of clinical factors associated with length of stay

Factor	LOS (days)	Hazard ratio (95%CI)	*P* value
Age (years)[1]			
< 70	7 (7, 9)	1.000 (reference)	
≥ 70	8 (7, 10)	1.216 (1.048-1.411)	0.010
Operation time (min)[1]			
< 160	7 (7, 8)	1.000 (reference)	
≥ 160	8 (7, 11)	1.431 (1.237-1.656)	< 0.001
Comorbidity			
0-2	8 (7, 9)	1.000 (reference)	
≥ 3	8 (7, 11)	1.067 (0.839-1.357)	0.595
PNI[1]			
≥ 44.5	8 (7, 11)	1.000 (reference)	
< 44.5	9 (8, 13)	1.792 (1.058-3.032)	0.030
Prealbumin (mg/L)			
≥ 180	8 (7, 9)	1.000 (reference)	
< 180	8 (7, 10)	0.797 (0.514-1.237)	0.312
Clavien-Dindo classification			
None	8 (7, 9)	1.000 (reference)	
I + II	10 (7, 12)	1.163 (1.163-1.701)	0.435
III or higher	10 (7, 17)	2.191 (1.604-2.991)	< 0.001

[1]Split at median.
LOS: Length of stay; PNI: Prognostic nutritional index.

0.001) were recognized as independent predictors for prolonged LOS of elderly patients with gastric cancer enrolled in this study.

DISCUSSION

Malnutrition presents a significant challenge to patient's safety in perioperative settings, particularly among elderly patients[18]. In elderly patients with gastric cancer, perioperative malnutrition often occurs due to decreased physical activity, absorption disorders, insufficient food intake, and metabolic disruptions[19]. These malnourished patients often develop anemia, hypoproteinemia, and electrolyte abnormalities before surgery[20]. Additionally, malnourished elderly patients always experience higher rates of postoperative complications and longer hospital stays compared to well-nourished individuals[21]. Hence, it is crucial to screen and assess the nutritional status of patients before major abdominal surgery. In our research, the overall frequency of malnutrition in elderly gastric cancer patients was 31.8%, which is relatively high compared to findings from previous research. This variation can be attributed to observed differences in age distribution, measuring instruments, patient characteristics, and hospital locations.

Preoperative malnutrition in patients is often indicated by lower levels of hemoglobin, prealbumin, and albumin compared to well-nourished individuals[22]. Selecting appropriate assessment tools is vital for the early diagnosis and

treatment of malnutrition. The PNI, determined by the concentration of serum albumin and lymphocyte count in peripheral blood, serves as an indicator of the inflammatory and nutritional status as well as patient prognosis[17]. Unlike other screening tools, PNI is advantageous as it can be swiftly and easily assessed *via* laboratory tests during the preoperative diagnosis. Previous studies have shown that preoperative PNI is an independent prognostic factor for disease-free survival together with the TNM stage in gastric cancer patients following surgery[23]. Recent research had identified preoperative PNI as a specific and sensitive prognostic predictor for elderly patients who underwent gastrointestinal tumor surgery[24]. Monitoring PNI indicators can help to predict malnutrition occurrence before surgery, guide prevention efforts and reduce perioperative complications in gastric cancer patients[25]. The results of this study revealed that low PNI is an independent predictor for prolonged hospital stays, suggesting that PNI predicts both short-term and long-term outcomes for elderly patients. Future research is essential to enhance the understanding and improvement of preoperative PNI.

Malnutrition, defined as a condition resulting from inadequate intake of minerals, vitamins, and other nutrients necessary for maintaining healthy tissues and organ function, requires collaborative efforts from healthcare providers, nurses, and access to nutritious food[15]. Providing nutritional support to malnourished patients can mitigate postoperative complications, such as surgical site infections and gastrointestinal issues after surgery[25]. Guidelines from the ESPEN and American Society for Parenteral and Enteral Nutrition recommend that it is preferable to use oral or enteral nutrition if at all possible[16,26]. Generally, enteral nutrition is preferred over parenteral nutrition because it is more physiological, cheaper, simpler, and less complicated. In addition, there are a large number of studies demonstrating that food in the gut has an important role in preserving normal physiology, especially that related to immune function and systemic inflammation[27]. However, in cases where a patient experiences pyloric obstruction or when enteral nutrition does not provide sufficient energy, alternative nutrition methods such as peripheral parenteral nutrition or TPN are often utilized. Our study found a significantly higher rate of preoperative TPN in malnourished patients compared to well-nourished patients, though the overall rate of preoperative parenteral nutrition support in malnourished patients was low (43.5%). Optimizing the nutritional status of elderly patients with malnutrition prior to surgery is essential for improving surgical outcomes.

Despite recommendations advocating for early initiation of oral or enteral feeding to enhance clinical outcomes and minimize surgical complications in gastric cancer patients postgastrectomy, postoperative nutritional support practices vary widely among different surgical teams. According to the Japanese Gastric Cancer Treatment Guidelines, liquids should be introduced on the first postoperative day, with solid foods starting from the second to fourth day, depending on the type of surgery[28]. In this study, the median duration of parenteral nutrition was five days. Notably, 54.8% of elderly patients received only carbohydrates, with or without composite amino acids postoperatively, several important insights and implications can be drawn regarding the nutritional management of these patients. No significant difference in duration was observed between well-nourished and malnourished patients. It may take time for malnourished patients to receive adequate care. Our study also confirmed previous findings that malnourished patients have higher overall postoperative complication rates. This underscores the need for heightened attention and individualized nutritional support for elderly patients during the postoperative period.

There are several limitations to this study. First, being a retrospective analysis, it may have selection biases despite data collection from a prospectively recruited database. Second, long-term outcomes were not considered, and the relationship between perioperative nutritional support and clinical outcomes in malnourished patients was not investigated. Third, there are many subjective factors which might affect length of hospital stay, such as the patient's subjective wishes, that were not included, and these may be as important as objective factors, particularly in China.

CONCLUSION

Malnutrition is relatively common in elderly patients undergoing gastrectomy. Low PNI is an independent risk factor associated with delayed discharge. More attention and strategies are needed to improve the clinical outcome of malnourished elderly gastric cancer patients.

FOOTNOTES

Author contributions: Zhao XN and Lu J collected and analyzed the data, wrote the manuscript; He HY and Ge SJ designed the study and edited the manuscript; Zhao XN and Lu J contributed equally to this work. All authors have read and approved the final manuscript. There are three main reasons for designating He HY and Ge SJ as co-corresponding authors. First, the research was a collaborative effort, and this designation accurately reflects the distribution of responsibilities and the significant time and effort each author devoted to completing the study and the resultant paper. Second, the research team comprised authors with diverse expertise and skills from different fields. The designation of co-corresponding authors best represents this diversity, promoting a comprehensive and in-depth examination of the research topic. Third, He HY and Ge SJ collaborated to design and refine the study protocol and contributed equally to reviewing and editing the manuscript. Recognizing these researchers as co-corresponding authors acknowledges and respects their equal contributions and highlights the spirit of teamwork and collaboration in this study. In summary, designating He HY and Ge SJ as co-corresponding authors accurately reflects our team's collaborative spirit, equal contributions, and diverse expertise, thereby enhancing the overall quality and reliability of the manuscript.

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