Preoperative Nutritional Deficiency Is a Useful Predictor of Postoperative Outcome in Patients Undergoing Curative Resection for Gastric Cancer

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Abstract

BACKGROUND: Preoperative nutritional deficiency (ND) has been shown to be a valuable prognostic factor in urologic malignancies. We aimed to investigate the prognostic value of ND in patients with gastric cancer (GC). *METHODS:* A single-center cohort of 1026 GC patients undergoing curative resection between 2003 and 2012 was categorized to ND and nutritionally replete (NR) groups. Patients with body mass index <18.5 kg/m^2, preoperative albumin <35 g/l, or preoperative weight loss ≥5% of body weight were defined as ND. *RESULTS:* Of the 1026 patients included in the study, 585 (57.0%) were categorized as ND. Overall survival (OS) at 5 years was 68.5% for ND patients and 44.0% for NR patients (*P* < .001). Multivariate analysis revealed that ND was a significant predictor of OS (hazard ratio: 1.954; 95% confidence interval: 1.552-2.460; *P* < .001). In stage-stratified analysis, it was still independently associated with OS in tumor-nodes-metastasis stage II and III (*P* = .004 and *P* < .001, respectively). Of note, the prognostic significance of ND was still maintained when stratified by age, sex, anemia, and adjuvant chemotherapy (all *P*s < .05). *CONCLUSION:* Preoperative ND is a novel predictor of outcome in GC, especially in stage II to III GC, and may help clinicians identify high-risk patients for proactive nutritional interventions.

Introduction

Over the past decades, the incidence and mortality rate of gastric cancer (GC) have been steadily decreased. However, GC is still one of the most common malignancies nowadays, with a high incidence of recurrence and metastasis even after curative resection [1,2]. In China, GC is the second leading cause of cancer death among both men and women in 2015 [3]. Despite advances in surgical techniques, the long-term postoperative survival of GC patients is still poor with the relatively late stage of diagnosis [4].

In many cancers, independent prognostic factors are useful for selecting high-risk patients and tailoring treatment. Currently, pathologic stage and lymph nodes status, which determine the GC American Joint Committee on Cancer stages, represent the gold standard for assessing GC prognosis after radical surgery [5]. However, many other tumor features have also been validated to play an important role in predicting the postoperative survival in GC. For example, systemic inflammatory response has been consistently recognized to confer poorer outcome in patients with various

cancers and become the hot topic for clinicians and researchers [6–8]. Moreover, cancer-associated malnutrition is also increasingly appreciated to have a major role [9,10]. Malnutrition, defined as a nutritional status in which there is a deficiency of energy, protein, and other nutrients, can negatively influence the defensive system in our body and may cause adverse clinical outcomes [11,12]. However, up to now, no ideal indices

exist to evaluate patients for preoperative nutritional risk [13]. In recent years, nutritional deficiency (ND), a nutritional-based index, has been demonstrated as a strong predictor of postoperative outcomes in urologic malignancies [14,15]. With regard to GC, the clinical significance and prognostic value of this index remain uncertain.

In the present study, we aimed to investigate the prognostic utility of preoperative ND, as measured by body mass index (BMI), serum albumin, and preoperative weight loss, in patients undergoing curative resection for GC.

Material and Methods

Ethics Statement
The study complied with the standards of the Declaration of Helsinki and was approved by the Research Ethics Committee at the Cancer Center of Sun Yat-sen University. Written informed consent was obtained from each patient.

Study Population
This study reviewed 1026 patients undergoing curative resection for GC at Cancer Center of Sun Yat-sen University between January 2003 and December 2012. All patients were histologically confirmed as having stage I to III gastric adenocarcinoma, with stage determined according to the 7th edition of the American Joint Committee on Cancer tumor-nodes-metastasis (TNM) classification [5]. According to current guidelines, patients with stage II or stage III GC and no significant comorbidities precluding chemotherapy use were offered primarily 5-fluorouracil–based adjuvant chemotherapy after surgery [16–18]. The exclusion criteria were as follows: 1) no entire set of clinicopathological and laboratory data, 2) neoadjuvant chemotherapy or radiotherapy, 3) preoperative nutritional intervention (e.g., albumin) within 1 month before surgery, and 4) clinical evidence of non–cancer-related malnutrition.

Data Acquisition
Clinicopathological and outcome data were collected by review of the medical records. Routine laboratory measurements, including the serum levels of carcinoembryonic antigen (CEA) and albumin, were carried out within 1 week before surgery. Unintentional preoperative weight loss within 6 months was recorded at the time of diagnosis. Regarding the histological grade, patients with papillary and well- or

Table 1. General Characteristics of 1026 GC Patients

	No. of Patients (%)
Age (y)	
< 60	544 (53.0%)
≥ 60	482 (47.0%)
Sex	
Female	326 (31.8%)
Male	700 (68.2%)
Tumor size (cm)	
<5	583 (56.8%)
≥5	443 (43.2%)
Tumor location	
Upper third	411 (40.1%)
Middle third	202 (19.7%)
Lower third	413 (40.3%)
Histological grade	
Well differentiated	175 (17.1%)
Poorly differentiated	851 (82.9%)
Anemia	
No	737 (71.8%)
Yes	289 (28.2%)
BMI (kg/m^2)	
<18.5	401 (39.1%)
≥18.5 to <25.0	351 (34.2%)
≥25.0	274 (26.7%)
Serum albumin (g/l)	
≥35	941 (91.7%)
<35	85 (8.3%)
Preoperative weight loss	
<5%	694 (67.6%)
≥5% to ≤10%	221 (21.5%)
>10%	111 (10.8%)
Nutrition status	
NR	441 (43.0%)
ND	585 (57.0%)
CEA	
Normal	742 (77.6%)
Elevated	214 (22.4%)
TNM stage	
I	177 (17.3%)
II	257 (25.0%)
III	592 (57.7%)
Adjuvant chemotherapy	
No	393 (38.3%)
Yes	633 (61.7%)

Table 2. Univariate and Multivariate Analyses of OS in 1026 Patients Undergoing Curative Resection for GC

	Univariate Analysis		Multivariate Analysis	
	HR (95% CI)	P Value	HR (95% CI)	P Value
Age (y)		<.001		<.001
<60	1.00		1.00	
≥60	1.462 (1.200-1.781)		1.556 (1.259-1.923)	
Sex		.188		
Female	1.00			
Male	0.870 (0.707-1.071)			
Tumor size (cm)		<.001		.705
<5	1.00		1.00	
≥5	1.915 (1.571-2.335)		1.044 (0.837-1.302)	
Tumor location		<.001		.003
Upper third	1.00		1.00	
Middle third	0.613 (0.467-0.804)	<.001	0.769 (0.578-1.025)	.073
Lower third	0.481 (0.384-0.602)	<.001	0.665 (0.522-0.847)	.001
Histological grade		.014		.015
Well differentiated	1.00		1.00	
Poorly differentiated	1.441 (1.077-1.929)		1.487 (1.081-2.046)	
Anemia		.006		.702
No	1.00		1.00	
Yes	1.349 (1.092-1.667)		1.045 (0.837-1.311)	
BMI (kg/m^2)		<.001		
<18.5	1.00			
≥18.5 to <25.0	0.817 (0.654-1.022)	.077		
≥25.0	0.593 (0.457-0.768)	<.001		
Serum albumin (g/l)		<.001		
<35	1.00			
≥35	2.362 (1.767-3.156)			
Preoperative weight loss		<.001		
<5%	1.00			
≥5% to ≤10%	2.156 (1.722-2.698)	<.001		
>10%	2.184 (1.635-2.918)	<.001		
Nutrition status		<.001		<.001
NR	1.00		1.00	
ND	2.326 (1.876-2.885)		1.954 (1.552-2.460)	
CEA		<.001		.364
Normal	1.00		1.00	
Elevated	1.665 (1.327-2.090)		1.114 (0.883-1.405)	
TNM stage		<.001		<.001
I	1.00		1.00	
II	2.970 (1.602-5.507)	<.001	2.429 (1.265-4.662)	.008
III	12.573 (7.219-21.896)	<.001	9.986 (5.537-18.008)	<.001
Adjuvant chemotherapy		.799		
No	1.00			
Yes	0.974 (0.794-1.194)			