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Original article

Prognostic significance of perioperative nutritional parameters in patients with gastric cancer

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SUMMARY

Background & aims: It has been suggested that nutritional status is related to the survival outcomes of cancer patients. The purpose of the current research is to evaluate the importance of the prognosis of various nutritional parameters during the perioperative period in patients with gastric cancer.
Methods: This study enrolled patients with gastric cancer who underwent D2 gastrectomy at the Department of Surgery, Samsung Medical Center, in 2008. The prognostic significance of nutritional parameters was analyzed, along with other clinical and pathological variables, preoperatively and postoperatively at 3, 6, and 12 months.
Results: The total number of patients was 1415. The mean values of nutritional parameters, weight, body mass index (BMI), hemoglobin, total cholesterol, and total lymphocyte count (TLC) decreased significantly over time after surgery. On the contrary, albumin and prognostic nutritional index (PNI) score increased significantly during the postoperative follow-up period. Preoperatively, low BMI (<18.5 kg/m^2) and low TLC level (<1000 per mm^3) were revealed as independent prognostic factors in multivariate analysis. Low preoperative TLC level and decline in PNI (ΔPNI < −2.2) at postoperative 3 months; low preoperative TLC level and decline in TLC (ΔTLC < −279.9 per mm^3) at postoperative 6 months; and low preoperative BMI, albumin, and TLC levels at postoperative 12 months were independent nutritional prognostic indicators.
Conclusion: Various perioperative nutritional parameters were confirmed as independent prognostic factors in patients with gastric cancer. Our results imply prognostic benefit from careful nutritional support for patients with poor nutritional parameters.

1. Introduction

The high frequency of gastric cancer deaths worldwide has driven investigation into effective prevention strategies to reduce gastric cancer mortality [1]. Many prognostic factors affect the survival of patients with gastric cancer [2], but most of them cannot be altered by physicians. Nutritional status could be an important amendable factor in the treatment and prognosis of patients. Previous work showed that poor nutritional state of surgical patients could influence both postoperative complication and survival [3]; thus, nutritional assessment of patients with gastric cancer is necessary in clinical practice, and deficiencies should be corrected.

A previous study evaluated the prevalence of perioperative malnutrition using objective variables (human body measurement and blood chemistry results) and subjective evaluation systems in gastric cancer patients undergoing curative resection [4]. It concluded that objective and subjective evaluations are needed to detect poor nutritional conditions early. Assessing nutritional status using characteristics of the patient's history and physical examination, such as the subjective global assessment questionnaire [5] and nutritional risk screening [6], might be effective for

Abbreviations: BMI, body mass index; LN, lymph node; PNI, prognostic nutritional index; TLC, total lymphocyte count.

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nutritional diagnosis; however, such assessments are rather difficult and complicated to use in clinical practice, and some of the parameters required are unavailable during the follow-up period.

Simpler and more convenient tools for nutrition assessment are body mass index (BMI) and serum proteins, such as albumin and prealbumin. Due to its simplicity of calculation with patient height and weight, BMI is commonly used as an indicator of obesity. Some reports showed favorable prognosis in perioperative obese patients after gastric cancer surgery [7,8]. Albumin has also been commonly used by doctors to determine the nutritional status of patients, and a study revealed that serum albumin is an important factor to predict prognosis in gastric cancer patients [9]. However, serum albumin level is a somewhat unreliable tool for malnutrition as it can be influenced by systemic inflammatory reactions [10,11]. Another available tool is the prognostic nutritional index (PNI), which can be determined with the serum albumin level and peripheral blood total lymphocyte count (TLC) [12]. Several studies have suggested that patients with low preoperative PNI had poor overall survival [13–16]. However, those studies are limited because they did not include other nutritional parameters alongside PNI in the analysis and did not evaluate the significance of postoperative PNI changes or the influence of adjuvant chemotherapy.

Our aim in the present study was to assess the perioperative nutrition status of gastric cancer patients who underwent radical gastrectomy and to investigate the prognostic significance of various nutritional parameters along with other significant clinical and pathological variables in those patients.

2. Materials and methods

2.1. Study design & subjects

The study analyzed 1644 patients with gastric cancer who underwent radical surgery at the Department of Surgery, Samsung Medical Center, in 2008. Those who were diagnosed with another malignancy or stage IV gastric cancer or who received neoadjuvant treatment were excluded. In this study, 1415 patients who underwent D2 lymphadenectomy and either subtotal gastrectomy with Billroth I/II reconstruction or total gastrectomy with Roux-en Y esophagojejunostomy were analyzed. Follow-up evaluations with clinical and laboratory examinations were conducted at outpatient visits 3 months (n = 991), 6 months (n = 759), and 12 months (n = 895) after the operation. Patients who were not diagnosed as early gastric cancer (stage T1N0 or T2N0) usually underwent adjuvant chemotherapy after the surgery.

2.2. Research instruments

The clinicopathological characteristics of age, sex, medical comorbidity, duration of chemotherapy, histologic type, tumor location, tumor size, depth of invasion, lymph node metastasis, pathologic stage, lymphatic involvement, venous involvement, and perineural involvement were reviewed. The pathological data were evaluated using hematoxylin and eosin (H&E) stain. Histologic type was categorized as differentiated or undifferentiated. Well or moderately differentiated adenocarcinoma were classified as differentiated, whereas poorly differentiated tubular adenocarcinoma, signet ring cell type, and mucinous adenocarcinoma were assigned to the undifferentiated group. The pathologic stage was classified according to the 8th edition of American Joint Committee on Cancer classification. Perioperative data were also noted, including method of operation, extent of resection, and combined resection. Nutritional assessment was performed perioperatively using the parameters of weight, BMI, hemoglobin, albumin, cholesterol, TLC, and PNI. We obtained this information from the baseline workup conducted within 3 months before and 3 months, 6 months, and 12 months after surgery. PNI was calculated by the following equation [(10 × serum albumin (g/dL)) + (0.005 × total lymphocyte count)]. We defined underweight patients as those whose BMI was under 18.5 kg/m^2 (commonly used as a cut-off level for Asians and proposed by the World Health Organization (WHO)). An albumin level below 3.5 g/dL is generally considered low (hypoalbuminemia) and requires replacement in clinical practice. In this study, we used the WHO hemoglobin thresholds to define anemia (12.0 g/dL for women, 13.0 g/dL for men). Hypocholesterolemia was defined when total cholesterol level was below 160 mg/dL, following the American Heart Association's 1994 guidelines. Hemoglobin level was measured by cyanide-free hemoglobin spectrophotometry, and cholesterol level was measured by enzymatic colorimetric method. We defined a TLC level below 1000 per mm^3 as lymphopenia [17]; this cut off level might reflect severe malnutrition and immune deficiency. There is controversy regarding the optimal cut-off values for PNI. A previous study of PNI concluded that surgery of the gastrointestinal tract can be performed safely when the index is over 45 [12]. In the present study, the PNI value for the 10th percentile (45.2) of the enrolled patients was used as a cut-off. To evaluate nutritional parameters as prognostic factors, the differences between preoperative and postoperative nutritional values of each patient were calculated, and

Table 1
Clinicopathologic characteristics of patients who underwent gastrectomy (n = 1415).

Variable	Value	Variable	Value
Age, yr	56.4 ± 12.0	Depth of invasion	
Age		T1	802 (56.7)
≥60yrs	602 (42.5)	T2	205 (14.5)
<60yrs	813 (57.5)	T3	264 (18.7)
Sex		T4	144 (10.2)
M	923 (65.2)	LN metastasis	
F	492 (34.8)	N0	923 (65.2)
Medical comorbidity		N1	183 (12.9)
No	913 (64.5)	N2	121 (8.6)
Yes	502 (35.5)	N3a	113 (8.0)
Method of operation		N3b	75 (5.3)
Open	1294 (91.4)	Pathologic stage[a]	
Laparoscope	121 (8.6)	I	886 (62.6)
Extent of resection		II	250 (17.7)
Subtotal	1087 (76.8)	III	279 (19.7)
Total	328 (23.2)	Lymphatic invasion	
Combined resection		Absent	905 (64.0)
No	1279 (90.4)	Present	510 (36.0)
Yes	136 (9.6)	Vascular invasion	
Postoperative complication		Absent	1318 (93.1)
No	1119 (79.1)	Present	97 (6.9)
Yes	296 (20.9)	Perineural invasion	
Chemotherapy		Absent	1114 (78.7)
No	917 (64.8)	Present	301 (21.3)
Yes	489 (34.6)		
Unknown	9 (0.6)		
Duration of chemotherapy (months)	8.5 ± 10.6		
Tumor location			
Whole	18 (1.3)		
Upper	165 (11.7)		
Middle	504 (35.6)		
Lower	728 (51.4)		
Tumor size, cm	4.2 ± 2.8		
Histologic type			
Differentiated	521 (36.8)		
Undifferentiated	894 (63.2)		

Values are presented as mean ± standard deviation or number (%).
[a] According to the 8th edition of the American Joint Committee on Cancer classification.

the mean value for use as a cut-off was determined. After this calculation, the patients were divided into 2 groups: those whose nutritional values decreased by more than the mean value were sorted into the high risk group. Complications that occurred in postoperative one month or during hospitalization were recorded as morbidity or mortality. We also included other postoperative complications that needed to be managed by readmission in the analysis.

2.3. Ethical approval

The study protocol was approved by the institutional review board of Samsung Medical Center, Seoul, Korea (SMC 2017-05-143).

2.4. Statistical analysis

Categorical continuous variables were analyzed using Student's t test. The values of the clinicopathologic characteristics are presented as mean ± standard deviation or number (%). The nutritional values of each period are presented as mean and standard deviation. Kolmogorov–Smirnov test was used to test the normality of the nutritional values in each period. The difference between two time points (preoperative and postoperative) was analyzed by paired t-test or Wilcoxon signed rank test according to the normality test results. P values were adjusted using Bonferroni's method in case of multiple testing. The generalized estimating equation approach was used to evaluate changes between

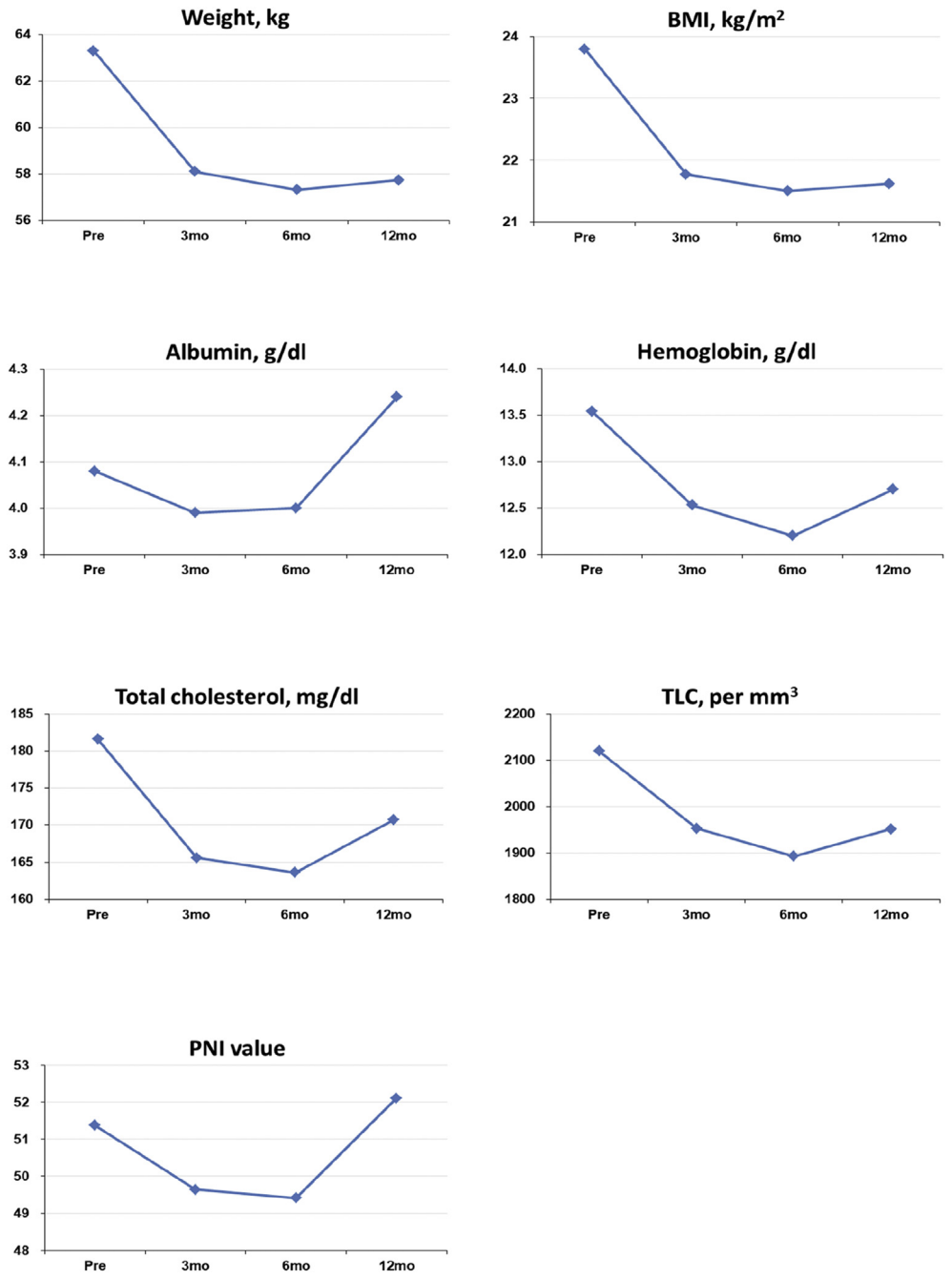

Fig. 1. The mean values of nutritional parameters of gastric cancer patients at preoperative and postoperative 3, 6, 12 months.

preoperative and postoperative (3, 6, and 12 months) nutritional values and to handle missing data during the follow-up period. The 5-year survival rate was calculated using the Kaplan–Meier method, and the log-rank test was used to determine the significance of the variables, described above. Variables with $p < 0.05$ in the univariable analysis by the Kaplan–Meier method were included in the multivariable analysis. Multivariable analysis was carried out using a Cox proportional hazards model with the backward logistic regression method to identify independent risk factors for patient survival. The hazard ratio and 95% confidence interval were calculated. $P < 0.05$ was considered statistically significant. Statistical analysis was carried out using SPSS® version 22.0 for Windows statistical software (SPSS, Chicago, IL, USA) and SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

3. Results

We included 1415 gastric cancer patients; their clinical, operative, and pathologic characteristics are reviewed in Table 1. The mean age of the study cohort was 56.4 ± 12.0. Most patients underwent open subtotal gastrectomy. 37.4% of the patients were diagnosed with stage II and III. The proportion of patients who received adjuvant chemotherapy is 34.6%. The perioperative nutritional characteristics of patients are shown in Fig. 1 and Table 2. The means for weight, BMI, hemoglobin, total cholesterol, and TLC decreased significantly over time. The means for albumin and PNI value increased significantly at postoperative 12 months compared to the preoperative state.

The clinicopathologic and nutritional prognostic factors that were significant in univariate analysis ($p < 0.05$) were included in the multivariate analysis for overall survival (Tables 3 and 4). The clinicopathologic factors that were significant in the overall multivariate analysis (preoperative and 3, 6, and 12 months postoperative) were postoperative complications, duration of chemotherapy, location of the tumor, depth of invasion, and lymph node metastasis. Patient age at the time of the operation was significant in the analysis of preoperative and postoperative 3 and 6 months data. In addition, the presence of perineural invasion was significant only 6 months after the operation. Though the presence of vascular invasion was significant in the preoperative and

Table 2
Nutritional characteristics of patients who underwent gastrectomy.

	Mean	SD	MD	Normality‡	p Value†	Beta coefficient	SE	p Value§
Weight, kg						−0.439	0.018	<0.001
Preoperative (1415)	63.3	10.6						
Postoperative								
3 months (1023)	58.1	9.6	−5.5	0.010	<0.001			
6 months (946)	57.3	9.7	−6.4	0.010	<0.001			
12 months (930)	57.7	9.9	−5.9	0.010	<0.001			
BMI, kg/m^2						−0.172	0.006	<0.001
Preoperative (1415)	23.8	3.0						
Postoperative								
3 months (1023)	21.8	2.6	−2.1	0.010	<0.001			
6 months (946)	21.5	2.7	−2.4	0.010	<0.001			
12 months (930)	21.6	2.7	−2.2	0.010	<0.001			
Albumin, g/dl						0.014	0.001	<0.001
Preoperative (1415)	4.1	0.4						
Postoperative								
3 months (1313)	4.0	0.3	−0.1	0.010	<0.001			
6 months (940)	4.0	0.3	−0.1	0.010	<0.001			
12 months (1049)	4.2	0.3	0.1	0.010	<0.001			
Hemoglobin, g/dl						−0.062	0.004	<0.001
Preoperative (1415)	13.5	2.0						
Postoperative								
3 months (1313)	12.5	1.6	−1.1	0.010	<0.001			
6 months (939)	12.2	1.6	−1.3	0.010	<0.001			
12 months (1048)	12.7	1.7	−0.9	0.010	<0.001			
Total cholesterol, mg/dl						−0.752	0.080	<0.001
Preoperative (1415)	181.6	34.9						
Postoperative								
3 months (1313)	165.6	30.3	−16.6	0.060	<0.001*			
6 months (938)	163.6	28.9	−17.8	0.088	<0.001*			
12 months (1050)	170.7	30.6	−12.4	0.010	<0.001			
TLC, per mm^3						−12.935	1.527	<0.001
Preoperative (1415)	2120.0	672.1						
Postoperative								
3 months (1313)	1952.8	818.3	−172.7	0.010	<0.001			
6 months (939)	1892.7	756.2	−233.3	0.010	<0.001			
12 months (1048)	1951.3	647.9	−180.7	0.010	<0.001			
PNI value						0.077	0.013	<0.001
Preoperative (1415)	51.4	5.2						
Postoperative								
3 months (1313)	49.6	5.3	−1.8	0.010	<0.001			
6 months (935)	49.4	5.7	−2.0	0.010	<0.001			
12 months (1048)	52.1	5.0	0.5	0.010	0.004			

Values in parentheses are the numbers of patients. Difference between two time points (preoperative and postoperative) was analyzed by *Paired t-test or †Wilcoxon signed rank test according to normality test (‡Kolmogorov–Smirnov) results. We used a §generalized estimating equation to deal with missing nutritional values; this model is known to be suitable in settings that use repeated measurements in clinical medicine. There are significant declines in the 3, 6, and 12 month postoperative nutritional values (weight, BMI, hemoglobin, total cholesterol, TLC) from the preoperative state. Abbreviations: BMI, body mass index; MD, perioperative mean difference; PNI, prognostic nutritional index; SD, standard deviation; SE, standard error; TLC, total lymphocyte count.

Table 3
Multivariate analyses of clinicopathologic prognostic factors of 5-year survival.

Variables	Preoperative (n = 1415)			Postoperative								
				3 months (n = 991)			6 months (n = 759)			12 months (n = 895)		
	HR	95% CI	p Value	HR	95% CI	p Value	HR	95% CI	p Value	HR	95% CI	p Value
Age (≥60 yrs/<60)	1.83	1.33–2.53	<0.001	1.92	1.32–2.81	0.001	1.96	1.31–2.93	0.001			
Sex (Male/Female)	–	–	–	–	–	–	–	–	–	–	–	–
Medical comorbidity (Yes/No)	–	–	–	–	–	–	–	–	–	–	–	–
Method of operation (Open/Laparoscope)												
Extent of resection (Total/Subtotal)												
Combined resection (Yes/No)	–	–	–	–	–	–	–	–	–	–	–	–
Postoperative complications (Yes/No)	1.88	1.36–2.60	<0.001	2.29	1.57–3.35	<0.001	2.49	1.66–3.72	<0.001	2.90	1.89–4.45	<0.001
Duration of chemotherapy			0.001			0.003			<0.001			<0.001
<6 months/No	0.57	0.37–0.89	0.013	0.82	0.42–1.59	0.557	0.44	0.20–0.93	0.031	0.78	0.36–1.69	0.523
≥6 months/No	1.11	0.72–1.71	0.635	1.67	0.86–3.21	0.129	1.02	0.48–2.17	0.959	2.32	1.11–4.87	0.025
Tumor location			<0.001			<0.001			<0.001			0.025
Middle/Lower	0.89	0.62–1.28	0.531	0.80	0.52–1.24	0.317	0.61	0.39–0.96	0.034	0.74	0.45–1.21	0.228
Upper/Lower	1.14	0.76–1.71	0.541	1.36	0.85–2.17	0.199	0.96	0.57–1.62	0.884	0.87	0.48–1.60	0.660
Whole/Lower	4.59	2.40–8.77	<0.001	5.17	2.65–10.07	<0.001	5.09	2.45–10.59	<0.001	3.15	1.36–7.32	0.008
Tumor size (≥5cm/<5)												
Histologic type (Differentiated/Undifferentiated)												
Depth of invasion			<0.001			<0.001			<0.001			<0.001
T2/T1	1.74	0.91–3.34	0.095	1.18	0.50–2.79	0.703	1.44	0.56–3.67	0.449	1.04	0.38–2.87	0.938
T3/T1	3.85	2.18–6.79	<0.001	3.07	1.48–6.40	0.003	3.36	1.45–7.78	0.005	2.86	1.20–6.79	0.017
T4/T1	5.51	2.97–10.22	<0.001	4.93	2.27–10.70	<0.001	4.71	1.89–11.74	0.001	4.71	1.92–11.58	0.001
LN metastasis			<0.001			<0.001			<0.001			<0.001
N1/N0	2.16	1.22–3.82	0.008	2.09	1.01–4.32	0.047	1.83	0.85–3.95	0.122	2.42	1.07–5.45	0.034
N2/N0	2.91	1.63–5.19	<0.001	1.85	0.86–4.00	0.116	1.67	0.75–3.72	0.209	3.26	1.44–7.41	0.005
N3a/N0	4.34	2.47–7.64	<0.001	3.94	1.93–8.01	<0.001	3.73	1.76–7.91	0.001	4.95	2.20–11.12	<0.001
N3b/N0	8.40	4.51–15.63	<0.001	6.15	2.90–13.06	<0.001	5.31	2.39–11.82	<0.001	5.40	2.19–13.34	<0.001
Pathologic stage[a]												
II/I												
III/I												
Lymphatic invasion (Yes/No)												
Vascular invasion (Yes/No)	1.51	1.03–2.23	0.037	1.84	1.20–2.84	0.006	1.70	1.07–2.70	0.024			
Perineural invasion (Yes/No)							1.63	1.06–2.51	0.026			

[a] According to the 8th edition of the American Joint Committee on Cancer classification. Abbreviations: CI, confidence interval; HR, hazard ratio; LN, lymph node; SE, standard error.

postoperative 3 and 6 months data analysis, it was not significant at postoperative 12 months (Table 3).

Preoperatively, low BMI status (<18.5 kg/m^2) and low TLC level (<1000 per mm^3) were significant, independent factors of poor prognosis. Three months after the operation, preoperative low TLC level and decline in PNI (ΔPNI < −2.2) were significant prognostic factors. Six months after the operation, preoperative low TLC level and decline in TLC (ΔTLC < −279.9 per mm^3) were significant prognostic factors. Twelve months after the operation, preoperative underweight, hypoalbuminemia and lymphopenia status were the significant prognostic factors among the nutritional parameters (Table 4).

Table 4
Multivariate analysis of nutritional prognostic factors of 5-year survival.

Variables	Preoperative (n = 1415)			Postoperative								
				3 months (n = 991)			6 months (n = 759)			12 months (n = 895)		
	HR	95% CI	p Value	HR	95% CI	p Value	HR	95% CI	p Value	HR	95% CI	p Value
Weight (<60 kg/≥60)	–	–	–	–	–	–	–	–	–	–	–	–
BMI (<18.5 kg/m^2/≥18.5)	1.97	1.02–3.83	0.044							2.30	1.01–5.25	0.048
Albumin (<3.5 g/dl/≥3.5)										2.21	1.21–4.01	0.009
Hemoglobin (Anemic/Non-anemic)												
Total cholesterol (<160 mg/dl/≥160)				–	–	–	–	–	–			
TLC (<1000 per mm^3/≥1000)	3.77	1.85–7.71	<0.001	5.22	2.11–12.91	<0.001	5.20	1.84–14.65	0.002	3.87	1.26–11.90	0.018
PNI value (<45.2/≥45.2)												
ΔWeight (<−5.5 kg/≥−5.5)				–	–	–				–	–	–
ΔBMI, (<−2.1 kg/m^2/≥−2.1)				–	–	–				–	–	–
ΔAlbumin, (<−0.1 g/dl/≥−0.1)				–	–	–	–	–	–	–	–	–
ΔHemoglobin, (<−1.1 g/dl/≥−1.1)										–	–	–
ΔTotal cholesterol, (<−16.9 mg/dl/≥−16.9)				–	–	–	–	–	–	–	–	–
ΔTLC, (<−251.8 per mm^3/≥−251.8)							1.88	1.23–2.89	0.004			
ΔPNI value (<−2.2/≥−2.2)				1.53	1.05–2.24	0.029				–	–	–

Δ means the difference between preoperative and postoperative nutritional parameters. We analyzed the mean Δ and divided patients into two groups to calculate 5-year survival using the Kaplan–Meier method. Abbreviations: BMI, body mass index; CI, confidence interval; HR, hazard ratio; PNI, prognostic nutritional index; SE, standard error; TLC, total lymphocyte count.

4. Discussion

In the present study, we identified five nutritional prognostic factors in surgical patients with gastric cancer. The significant nutritional prognostic factors differed at each follow-up period: 1) preoperative lymphopenia at the preoperative period and at postoperative 3, 6, 12 months, 2) preoperative underweight status preoperatively and at postoperative 12 months, 3) a decline in PNI value at postoperative 3 months, 4) a decline in TLC value at postoperative 6 months, and 5) preoperative hypoalbuminemia at postoperative 12 months. Apparently, declines in PNI and TLC values were prognostic factors for the short-term period after surgery, when the status of patients can be unstable and affected by surgical recovery, diet adaptation, adjuvant chemotherapy, tumor progression, etc., whereas preoperative TLC and BMI status seems to be prognostic factors for a rather more stable period.

In this study, patients who were underweight (BMI < 18.5 kg/m^2) prior to surgery showed worse overall survival in the multivariate analysis (HR 1.97; 95% CI 1.02–3.83; p = 0.044). Some studies have found that obese patients showed some morbidity and inadequacy of lymph node dissection; however, there was no significant difference in gastric cancer survival [18,19]. This result differed from that of other studies in Korea and Japan. A Korean study reported that BMI at the first year after surgery seemed to predict survival, but preoperative BMI was not an independent prognostic factor for gastric cancer patients [7]. Especially in early gastric cancer, the 5-year survival rate was better in preoperative obese patients than in non-obese patients in a Japanese study [8]. The influence of BMI on gastric cancer prognosis remains controversial. However, in our multivariate analysis, preoperative BMI status was found to be an important prognostic factor. Preoperative BMI status might correlate with individual physical recuperative ability and stress tolerance, which are important factors during the period of postoperative recovery and adjuvant therapy.

TLC has also been used as an important indicator of nutritional status and immune status. Malnourished patients are immunosuppressed and have a high risk of serious infection that can lead to morbidity and mortality [3]. TLC might reflect this pathophysiology better than any other nutritional parameter. A decrease in TLC to less than 1500/mm^3 or less than 900/mm^3 has been reported to reflect malnutrition or severe malnutrition, respectively. However, TLC might not be an appropriate indicator of malnourished old patients, among which it may reflect age rather than nutritional status [20,21].

A previous study used the PNI value for the 10th percentile of Korean gastric cancer patients (n = 7781) as a cut-off value for dividing patients into risk stratified PNI groups. They revealed that low preoperative PNI values (<46.70) could be used as an independent prognostic factor for overall survival (HR 1.383, 95% CI = 1.221–1.568, p < 0.001) [13]. In this regard, we used the 10th percentile (45.2) of our study cohort to stratify the patients into preoperative high and low PNI groups. However, this cut-off value was not a significant prognostic factor in our study. Instead, we found that patients whose preoperative TLC level was lower than 1000 per mm^3, defined as lymphopenia [17], had an unfavorable prognosis. There might be some limitations to using serum albumin as a nutritional parameter, and this weakness probably affects the preoperative PNI value, which is calculated using serum albumin and TLC. Albumin is commonly used as a conventional indicator of nutritional status, but it is also considered a negative acute phase protein, and its level is influenced by systemic inflammation and medication. A post-surgical state and cancer have both been shown to lower the albumin level. Because the diverse pathophysiology of many diseases influences the level of albumin, it is an indefinite marker for malnourished ill persons [10].

Few studies have evaluated postoperative changes in nutritional parameters. Our study assessed perioperative differences in various nutritional parameters and revealed that prognosis was affected by PNI changes at postoperative 3 months and TLC changes at postoperative 6 months. Patients whose PNI value decreased by more than 2.2 (at postoperative 3 months) and those with TLC value decreased by more than 279.9 per mm^3 (at postoperative 6 months) showed poor prognosis. These cut-off values could alert surgeons about need for nutritional support and what interventions might be meaningful during the short-term follow-up period.

As in any other retrospective study, the limitations of the current analysis include possible selection bias and detection bias. However, we examined a large number of patients using numerous basic nutritional parameters and evaluated not only preoperative nutritional values, but also perioperative change in those factors in order to determine their prognostic significance.

4.1. Conclusion

In conclusion, we identified perioperative nutritional parameters in patients with gastric cancer through multivariate analysis: preoperative BMI status, preoperative TLC level, preoperative albumin level, postoperative changes in PNI, and postoperative changes in TLC which represent the patient's nutritional and inflammatory status may act as prognostic indicators independently of other known clinical- and pathological prognostic factors. Our results imply that these nutritional parameters might be able to stratify high risk patients with poor perioperative nutritional status, and the prognostic benefit of careful nutritional support for such patients is expected.

Conflicts of interest

The authors declare that they have no conflict of interest.

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Ethical standards

This article does not contain any studies with human or animal subjects performed by any of the authors.

Author contributions

Min-Gew Choi and Jeong-Meen Seo designed and conducted this research. Min-Gew Choi and Sung Eun Oh analyzed data and wrote the paper. Min-Gew Choi had primary responsibility for final content. All authors read and approved the final manuscript.

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