Predicting Postoperative Events in Patients With Gastric Cancer: A Comparison of Five Nutrition Assessment Tools

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Abstract. *Background/Aim:* We compared the adequacy of five nutrition assessment tools with respect to their predictive value in patients with locally advanced gastric cancer (GC) receiving radical surgery. *Patients and Methods:* Five nutrition assessment tools—Glasgow prognostic score (GPS), malnutritional universal screening tool (MUST), nutritional risk screening, patient generated subjective global assessment (PG-SGA), and prognostic nutritional index (PNI)—were assessed preoperatively for stage III GC patients. The correlation between postoperative events and nutritional status was further analyzed. *Results:* Most of the nutritional tools accurately predicted length of hospital stay and grade 3 or higher surgical complications, while only the GPS correlated with 30-day readmission and surgical complications. The PG-SGA performed the poorest among the five tools and failed to predict any postoperative event. *Conclusion:* The application of GPS is recommended as a

prognostic index for patients with locally advanced GC prior to radical surgery.

While the treatment of *Helicobacter pylori* infection has decreased the prevalence of gastric cancer (GC), it remains the fifth most common cancer and was the third leading cause of cancer-related deaths worldwide in 2018 (1, 2). The asymptomatic nature during early stage contributes to its delayed diagnosis and the eventual poor prognosis (3). As radical surgery is the only potential cure for locally advanced GC, nutrition becomes a foremost concern as preoperative malnutrition is well recognized as a risk factor for postoperative morbidity and mortality (4, 5).

In cancer patients, malnutrition is often associated with anorexia-cachexia syndrome, characterized by decreased food intake, hypoalbuminemia, weight loss, and muscle tissue wasting (6). While malnutrition is prevalent among patients with advanced malignancy, malnutrition's prognostic role toward postoperative complications or long-term outcome is cancer-type dependent (7). This may be due to the absence of a universal definition of malignancy-related malnutrition and malnutrition's various contributing roles in different cancer types. Malnutrition is prevalent among GC patients due to its advanced stage at diagnosis and the tumor's anatomical location (8). The obstruction of the upper digestive tract directly impedes adequate oral intake which predisposes patients to further nutritional depletion. Despite its curative purpose for GC, gastrectomy is considered a major surgery often that leads to physical stress and wound

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healing, which drives patient's body into a hypermetabolic and catabolic state that may aggravate malnutrition (9). During the treatment of GC, malnutrition is often even more aggravated since vitamin B-12 and iron deficiency are common metabolic sequelae of gastrectomy (10).

In recent clinical practice, nutrition assessment tools that incorporate inflammation factors, such as Glasgow prognostic score and prognostic nutritional index, have also been developed to predict the postoperative morbidity and mortality of various cancers after radical surgeries (11-16). While previous studies have investigated the association between nutrition assessment tools and postoperative complications in GC patients, the results are inconclusive (10, 17). The nutrition assessment tools consist of heterogeneous, subjective items, and there is no consensus on the optimal nutrition tool for predicting postoperative complications for locally advanced GC (17, 18). Therefore, this retrospective single-center observational study was designed to assess the prognostic value of different nutrition assessment tools based on malnutrition or systemic inflammatory response in patients with locally advanced GC receiving radical surgery.

Patients and Methods

Patient selection and treatment. In total, 509 consecutive patients with stage III GC who underwent radical gastrectomy and D2 lymph node dissection surgery between 2007 and 2014 at Linkou Chang Gung Memorial Hospital were retrospectively analyzed. Tumor staging was defined according to the 7th edition of the American Joint Committee on Cancer (AJCC) staging system after pathological examination. Patients who underwent palliative surgery, received induction chemoradiotherapy before surgery, or had concurrent active malignancy were excluded. Patients with all the parameters required for Glasgow prognostic score (GPS), malnutritional universal screening tool (MUST), nutritional risk screening (NRS 2002), patient-generated subjective global assessment (PG-SGA), and prognostic nutritional index (PNI) were included. In total, 272 patients were included in the final analysis. For every nutrition assessment tool, patients were stratified into either well-nourished or malnourished status while the cutoff was defined by data obtained from previous studies (19-23). As the patients were stratified into two groups by the five respective nutrition assessment tools, the correlation between postoperative events and nutritional status was further analyzed.

Whether a patient should undergo total or subtotal gastrectomy was decided by the surgeon, based on tumor location and resection margin. This study was approved by the Institutional Review Boards of all the CGMH branches and was performed in compliance with the Helsinki Declaration (1996).

Data collection and follow-up. The details of the study have been described in our previous study (24). In brief, patient and tumor characteristics were retrospectively collected from a prospectively maintained electronic medical record. Subjective variables required for the nutrition assessment tools were obtained from patients or caregivers and clinical laboratory data (complete blood count,

Table I. Score range and data requirement of different nutrition screening tools.

	GPS	MUST	NRS2002	PG-SGA	PNI
Score range	0-2	0-6	0-7	0-46	*
Cutoff score for malnutrition	≥1	≥2	≥3	≥9	≤45
Objective variable					
Age			v	v	
CRP	v				
Albumin	v				v
Lymphocyte					v
BMI		v	v		
BWL		v	v	v	
Disease severity		v	v		
Subjective variable					
Loss of appetite			v	v	
Symptoms				v	
Physical activity				v	

*Range of PNI is undefined due to its dependence on albumin and lymphocyte levels. GPS: Glasgow prognostic score; MUST: malnutritional universal screening tool; NRS: nutritional risk screening; PG-SGA: patient generated subjective global assessment; PNI: prognostic nutritional index; CRP: c-reactive protein; BMI: body mass index; BWL: body weight loss.

biochemistry including serum albumin and C-reactive protein) were acquired prior to surgery. All postoperative events, including (length of hospital stay) LOS, surgical complication, postoperative 30-day readmission rate, and surgical mortality were recorded by retrospective chart review. Surgical complications were defined using the Clavien-Dindo Classification, which classified complications of grade 3 or higher as severe complications (25). The overall survival time was defined as the time from the date of surgery to the date of death by any cause or the last objective information registered in the medical chart. All patients were followed up until death or until 6/30/2016.

Glasgow prognostic score. A GPS score, calculated from the C-reactive protein (CRP) and albumin levels obtained prior to surgery, was assigned to each patient. Patients with both an elevated CRP (>10.0 mg/dl) and hypoalbuminemia (<3.5 g/dl) were assigned a score of 2 (19). Patients with only one of the two abnormal value were assigned a score of 1. Patients who had both CRP and albumin levels within normal ranges were assigned a score of 0. Patients with a GPS score ≥1 were assigned to the malnourished group.

Malnutritional universal screening tool. The MUST score is calculated by patient's BMI, unplanned weight loss, and acute disease effect (20). While a score is assigned for each category, MUST score is the sum of the scores where a value ≥2 is deemed as high risk of malnutrition and patients with such scores were assigned to the malnourished group in our study.

Nutritional risk screening. In nutritional risk screening, patients were scored for each of the two components, 1) nutritional status (BMI and weight loss) and 2) disease severity, according to whether they are absent, mild, moderate, or severe, resulting in a combined

Table II. Clinicopathological characteristics of the 272 patients with stage III gastric cancer.

Characteristic	N (%)
Median age, year (range)	65.7 (26.3-97.2)
Male sex	176 (64.7)
ECOG performance scale	
0 or 1	216 (79.4)
2	44 (16.2)
3	12 (4.4)
Charlson comorbidity index	
0	120 (44.1)
1	97 (35.7)
2	35 (12.9)
>2	20 (7.4)
Median BMI, kg/m ² (range)	22.2 (14.2-33)
Body weight loss	
<5%	176 (64.7)
≥5%	96 (35.3)
CEA, ng/dl	
<5	231 (84.9)
≥5	41 (15.1)
CA19-9, ng/dl	
≤37	223 (82.0)
>37	49 (18.0)
T-classification	
2	9 (3.3)
3	101 (37.1)
4	162 (59.6)
N-Classification	
0	44 (1.5)
1	18 (6.6)
2	77 (28.3)
3a	103 (37.9)
3b	70 (25.7)

ECOG: Eastern Cooperative Oncology Group; BMI: body mass index; CEA: carcinoembryonic antigen; CA19-9: carbohydrate antigen 19-9; AJCC: American Joint Committee on Cancer.

score of 0-6 (21). Patients with a total score of ≥3 were classified as nutritionally at-risk in the original design and assigned to the malnourished group in our study.

Patient generated subjective global assessment. The PG-SGA score is composed of patient-generated historical components (weight history, food intake, symptoms, activities and function) and professional assessment (diagnosis, age, metabolic stress, and physical exam) (22). A numeric score ≥9 required nutrient intervention in the original design, and these patients were assigned to the malnourished group in our study.

Prognostic nutritional index. The PNI was calculated using the following formula: $10 \times \text{serum albumin value (g/dl)} + 0.005 \times \text{total lymphocyte count in the peripheral blood (per mm}^3\text{)}$ (23). Patients with PNI lower than 45 were considered malnourished in our study.

Summary of nutrition assessment tools. Data requirements for each nutrition assessment tool are presented in Table I. Of the five nutrition assessment tools, GPS, MUST, and PNI required only

Table III. Statistical significance of correlation between patient characteristics and nutritional parameters.

Item	GPS	MUST	NRS 2002	PG-SGA	PNI
N of malnutrition patients (%)	172 (63.2%)	118 (43.4%)	56 (20.6%)	72 (26.8%)	58 (21.3%)
Age (≥65 years old)	0.07	0.37	*	0.12	0.013
BMI (≤18.5 kg/m ²)	0.18	<0.001	0.17	0.23	0.91
BWL (≥5%)	<0.001	*	*	*	0.64
CRP (≥10 mg/l)	*	0.017	0.014	0.79	0.038
Albumin (≤3.5 gm/dl)	*	0.021	<0.001	<0.001	*
Lymphocyte (≥10000/μl)	0.09	0.31	0.65	0.96	*
CEA (≥5 ng/ml)	0.98	0.54	0.55	0.44	0.19
CA19-9 (>37 U/ml)	0.32	0.58	0.13	0.08	0.004
ECOG (0,1 vs. 2,3)	0.026	0.18	<0.001	0.18	0.30
CCI	0.26	0.16	<0.001	0.31	<0.001
T-classification	0.002	0.08	0.75	0.86	0.17
N-Classification	0.81	0.60	0.55	0.08	0.90
AJCC tumor stage	0.002	0.008	0.26	0.11	0.21
Operation method	0.44	0.024	0.20	0.66	0.18
Resection margin	0.011	<0.001	0.002	0.13	0.70

*Denotes variable originally designated from the respective nutrition assessment tool; thus, the significance of the correlation was not calculated. BMI: Body mass index; BWL: body weight loss; CRP: C-reactive protein; CEA: carcinoembryonic antigen; CA19-9: carbohydrate antigen 19-9; ECOG: Eastern Cooperative Oncology Group; CCI: Charlson comorbidity index; AJCC: American Joint Committee on Cancer; GPS: Glasgow prognostic score; MUST: malnutritional universal screening tool; NRS 2002: nutritional risk screening; PG-SGA: patient generated subjective global assessment; PNI: prognostic nutritional index.

clinical data or assessment, while NRS2002 and PG-SGA also relied on information from patients or caregivers.

Statistical analysis. Demographic data were analyzed as median and 95% confidence intervals (CI). The differences between the nutritional status/clinical variables and postoperative adverse event was determined using the Pearson chi-squared (χ^2) test or Fisher's exact test. SPSS 17.0 software (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. All statistical assessments were two sided, and a *p*-value of <0.05 was considered statistically significant.

Results

Patient's basic characteristics are presented in Table II. Of the 272 included patients, 176 were men and 96 were women. The median age was 65.7 years (range=26.3-97.2) and 79.2% of the patients had an Eastern Cooperative Oncology Group (ECOG) performance of 0 or 1. The prevalence of malnutrition according to each nutrition assessment tool was 63.2%, 43.4%, 20.6%, 26.8%, and 21.3% according to GPS, MUST, NRS 2002, PG-SGA, and

Table IV. Statistical significance of correlation between nutritional parameters and postoperative events (n=461).

N of events (%)	LOS 20 (18-22)*	30-day readmission 34 (12.5%)	Surgical mortality 7 (2.6%)	Any surgical complication 111 (40.8%)	Surgical complication ≥grade 3 48 (17.6%)
Single item					
Age ≥65 years	0.004	0.039	0.28	<0.001	0.007
CRP ≥10 mg/l	0.001	0.003	0.14	0.001	0.005
Albumin ≤3.5 gm/dl	0.32	0.48	0.010	0.38	0.25
Lymphocyte ≥10000/μl	0.25	0.21	0.31	0.28	0.15
BMI ≤18.5 kg/m ²	0.40	0.07	0.31	0.68	0.99
BWL ≥5%	<0.001	0.99	0.22	0.47	0.09
Nutritional tool					
GPS ≥1	0.001	0.013	0.21	0.006	0.001
MUST ≥2	0.001	0.52	0.46	0.23	0.047
NRS2002 ≥3	0.001	0.36	0.14	0.12	0.044
PG-SGA ≥9	0.38	0.64	0.92	0.44	0.75
PNI >45	0.033	0.14	0.64	0.92	0.39

*Indicates median (95% confidence interval). Statistically significant differences are shown in bold. LOS: Length of hospital stay; CRP: C-reactive protein; BMI: body mass index; BWL: body weight loss; GPS: Glasgow prognostic score; MUST, malnutritional universal screening tool; NRS 2002: nutritional risk screening; PG-SGA: patient generated subjective global assessment; PNI: prognostic nutritional index.

PNI, respectively. The variables needed for the nutrition assessment tools were also examined. In the whole cohort, C-reactive protein (CRP) levels were >10 ng/dl in 58.8% of patients and hypoalbuminemia (<3.5 g/dl) was noted in 19.1% of patients. The median body mass index was 22.2 kg/m² and more than a third of the patients experienced body weight loss ≥5%.

Table III presents the statistical significance of correlation between patient characteristics and nutrition assessment tools. Apart from the variables originally designated from the respective nutrition assessment tools, several parameters showed significant correlation between patient characteristics and the nutrition assessment tool. GPS showed statistical correlation with body weight loss ($p<0.001$), ECOG performance ($p=0.026$), T-classification ($p=0.002$), AJCC tumor stage ($p=0.002$), and resection margin ($p=0.011$). MUST showed correlation with CRP ($p=0.017$), albumin ($p=0.021$), BMI ($p<0.001$), AJCC tumor stage ($p=0.008$), operation method ($p=0.024$), and resection margin ($p<0.001$). NRS 2002 showed correlation with CRP ($p=0.014$), albumin ($p<0.001$), ECOG ($p<0.001$), CCI ($p<0.001$), and resection margin ($p=0.002$). PG-SGA showed correlation with albumin ($p<0.001$). PNI was correlated with age ($p=0.013$), CRP ($p=0.038$), CCI ($p<0.001$), and CA19-9 ($p=0.004$).

Significance between postgastrectomy events and nutritional parameters is presented in Table IV. While age and CRP levels were correlated with 30-day readmission ($p=0.039$, $p=0.003$, respectively), surgical complications ($p<0.001$, $p=0.001$, respectively), and complication grading >3 ($p=0.007$, $p=0.005$, respectively), albumin levels were correlated with surgical mortality ($p=0.010$). Furthermore, CRP and BWL were both correlated with LOS ($p=0.001$,

$p<0.001$, respectively). Meanwhile, leukocytosis did not correlate with any postoperative events. Of the nutrition assessment tools, GPS was correlated with 30-day readmission ($p=0.013$), surgical complication ($p=0.006$), and complication grading ($p=0.001$). MUST and NRS 2002 showed correlation with complication grading of >3 ($p=0.047$, $p=0.044$). All the nutrition assessment tools except PG-SGA correlated with LOS. PG-SGA showed no correlation with any of the short-term postoperative events.

Discussion

While malnutrition and malignancy are frequently related, the prognostic role of malnutrition in many specific cancers is often undefined. A convenient nutrition assessment tool with good prognostic value may be beneficial for medical decision making. Few studies have made direct comparisons among different nutrition assessment tools regarding their prognostic value in predicting the postoperative complications in GC patients after radical gastrectomy (17, 18, 26). To identify the best correlating parameter to malnutrition in locally advanced GC, this study cross-analyzed five common nutrition assessment tools—GPS, MUST, NRS 2002, PG-SGA, and PNI—with the parameters used within each nutrition assessment tool. Comprehensive nutritional data were collected retrospectively from 272 patients with stage III GC treated at a high-volume medical center in Taiwan. This study revealed the significant prevalence of malnutrition among patients initially diagnosed with locally advanced GC, ranging from 20.6% to 63.2%, as evaluated by the different nutritional assessment tools. Furthermore, GPS was the most sensitive and useful tool for

predicting short-term events in terms of LOS, 30-day readmission rate, surgical complication, and severe surgical complications of gastrectomy. Both MUST and NRS showed prognostic value in predicting the LOS and severe surgical complications of gastrectomy. PNI showed correlation with LOS while PG-SGA failed to determine any short-term complications. While PG-SGA has been a valued prognostic tool in general oncology practice, it predominantly relies on subjective answers from patients compared to other nutritional tools. PG-SGA's inability to demonstrate significance in this study may due to the introverted nature of Taiwanese patients that may have affected the end score of the PG-SGA.

Different nutrition assessment tools require different sources of data input. Three of five tools, including GPS, MUST, and PNI, solely used objective variables for nutrition assessment, while the other two (NRS 2002 and PG-SGA) involved both objective and subjective variables for assessment. Subjective variables often entail patient participation, which may be time consuming and require extra manual work force. They may also yield high variance due to patients' different perceptions of sensation and unaccounted emotional weight. Thus, this might explain the unsatisfactory predictive value of the NRS 2002 and PG-SGA in our study.

To further distinguish the nutrition assessment tools, this study cross-analyzed the individual parameters used within the five nutrition assessment tools and the nutrition assessment tools themselves. Among the evaluated parameters, albumin, BWL, and CRP were prominent factors that correlated with the nutrition assessment tools. Apart from the GPS and PNI, which originally incorporated albumin for evaluation, albumin revealed independent association with MUST, PG-SGA, and NRS. CRP, which reflects systemic inflammation, also revealed independent relevance with MUST, NRS, and PNI. As BWL is incorporated in MUST, NRS, and PG-SGA, reflecting its importance in the evaluation of malnutrition, BWL was also independently associated with elevated GPS. Even though BMI showed relevance with MUST score, MUST incorporated BWL, which may confound the correlation since BWL and BMI both rely heavily on weight measurements. While these nutrition assessment tools have shown prognostic value in various cancers, albumin, BWL, and CRP stand out among the cross-analyzed parameters in the case of locally advanced GC. This may be explained by albumin, BWL, and CRP's significant reflection of malnutrition and systemic inflammation according to previous studies (7, 15, 20).

The associations between the short-term postoperative events and the individual parameters used in each nutrition assessment tool were also analyzed. While albumin and CRP were independently associated with different aspects of

short-term postoperative events, GPS, which incorporated both albumin and CRP, stood out among the nutrition assessment tools and showed the best correlation with short-term postoperative events. The NRS and MUST both showed prominence in predicting surgical complication grade of >3. However, GPS stood out in 4 of the 5 events and had *p*-value of 0.001 in predicting surgical complication grade of >3. Interestingly, all the nutrition assessment tools except PG-SGA correlated with LOS. Even though one out of the five postoperative outcomes showed correlation with almost all the nutrition assessment tools, this nonetheless demonstrates the ability of nutrition assessment tools to recognize malnourished patients who may need extra medical attention during their hospital stay.

While both the GPS and PNI consider only objective variables, they also include albumin as one of the parameters. Interestingly, the PNI did not demonstrate predictive value for any postoperative events in this study. However, a study by Lee *et al.* demonstrated the significance of PNI in predicting short- and long-term postoperative outcomes in a large number of studies (23). Our study and Lee's study both signify albumin's prognostic value. As both CRP and lymphocytes account for inflammatory response, we believe that inflammatory response contributed to its prognostic value along with malnutrition. The discrepancy between the two studies may due to the smaller study sample in our study. While the prognostic value of GPS is pronounced in this study, a study with a larger cohort to verify the prognostic value of GPS is encouraged.

Our previous study has indicated that patients with GPS 2 had an appalling in-hospital mortality rate of 10%, while for patients with GPS 0 and GPS 1, the in-hospital mortality rates were 1.0% and 1.5% respectively ($p=0.006$), indicating ostensibly poor prognosis surgery in patients with GPS 2 (24). However, no in-hospital mortality was observed in association with the GPS in this study. The reason for the discrepancy between the two studies is the simplification of the nutrition assessment tools that was necessary for this study. As mentioned in the methods, for the purpose of comparisons among the nutrition assessment tools, this study set a mandatory cutoff for each nutrition assessment tool. Thus, patients were distinctly categorized into the normal nutrition or malnourished groups by each tool. This study examined GPS score of 0 *vs.* GPS score of 1 and 2, whereas previous studies have evaluated the three different scores independently. As a result, the significance of in-hospital mortality of GPS in this study was statistically underestimated. Thus, it may be implied that among the nutrition assessment tools, GPS was found to be prominently associated with short-term postoperative risks of all aspects in patients with stage III GC.

In locally advanced GC, albumin and CRP levels may be evaluated alternatively alongside nutrition and common

prognostic guides. In addition to GPS, lower albumin levels also showed statistical significance with all the other nutrition assessment tools. Elevated CRP levels were also associated with malnutrition in the MUST, NRS, and PNI. While these nutrition assessment tools showed prominence in other fields of practice, correlation of albumin and CRP with these nutrition assessment tools suggested that they are accountable nutritional evaluation parameters. Thus, by combining the two parameters, GPS served as a reliable nutrition assessment tool with good prognostic value. Our study also revealed that elevated GPS is also significantly associated with some of the most common prognostic tools, such as body weight loss, ECOG, and tumor stage. This association may be attributed to the fact that these factors along with GPS are reflective of either tumor burdens, malnutrition, or disease severity, all of which lead to poor prognosis. Our previous study used multivariate analysis to show that GPS correlates with postoperative events independently of BWL, ECOG, and tumor stage (24). Thus, we suggest that GPS can be used as an additional guide for predicting prognosis of locally advanced GC.

While this study did not compare the five nutrition assessment tools' role in predicting overall survival, we believe that if a nutrition assessment tool does not provide postoperative prognostic benefit, its contribution to overall survival may be even more limited. As our previous study has explored the role of GPS in both short-term postoperative and long-term survival settings, the present study solidifies GPS's prognostic value among the different nutrition assessment tools.

Regardless of its strengths, this study has several limitations. First, as an analysis that relied partially on accurate record keeping, the retrospective design of this study had limited control over standardizing nutrition evaluation and initial outcome assessment. Second, given its single-center design, the outcome of this study may need to be externally validated, especially to confirm the performance of the PG-SGA in predicting postoperative adverse events in patients with GC as it showed no significant prognostic value in this study. Furthermore, patient selection bias may be present since patients with operable GC who decided against surgery and patients in whom metastasis was discovered perioperatively were excluded. With GPS's easy accessibility, future study goals may extend the use of GPS in patients with early GC or cancer of other origins.

Conclusion

Among the five commonly used nutrition assessment tools, GPS is most prominently associated with short-term postoperative risks of all parameters in patients with stage III GC. Furthermore, as it incorporates only objective values,

the GPS is easily accessible during clinical practice. This study supports the application of GPS in locally advanced GC patients prior to surgery.

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Conflicts of Interest

The Authors declare that no competing interests exist in relation to this study.

Authors' Contributions

Conception and design: Hsueh SW, Hsueh WH, Chou WC; Provision of study materials or patients: Liu KH, Tsai CY, Hsu JT; Collection and assembly of data: Hung CY, Tsang NM.

Data analysis and interpretation: Yang C, Chou WC; Final approval of manuscript: All Authors.

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