

Clinical Significance of the Geriatric Nutritional Risk Index in the Evaluation of Outcomes of Patients After Radical Gastrectomy

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Abstract

Background/Aim: The clinical evaluation of the GNRI in nutritional status management has been reported in several malignancies. This study aimed to investigate the relationship between the GNRI and clinical outcomes in postoperative patients who underwent radical gastrectomy.

Patients and Methods: Clinical data of 940 gastric cancer patients who underwent radical gastrectomy at Kanagawa Cancer Center from 2013 to 2020 were retrospectively collected and divided into a high-GNRI group (≥ 98) and a low-GNRI group (< 98) according to the GNRI. The association between the GNRI and overall survival (OS) and recurrence-free survival (RFS) was investigated.

Results: The respective 3- and 5-year OS rates were 92.0% and 86.3% in the high-GNRI group and 82.4% and 73.2% in the low-GNRI group ($p < 0.001$). A multivariate analysis showed that the GNRI was an independent predictor of the OS and RFS.

Conclusion: GNRI is an objective, noninvasive, and easily accessible prognostic biomarker for gastric cancer patients. Patient stratification using the GNRI and preoperative nutritional interventions may improve prognosis.

Keywords: GNRI, gastric cancer, survival, recurrence.

Introduction

Gastric cancer ranked fifth among new cancer cases and causes of death worldwide in 2022 (1). Radical resection

with lymph node dissection and perioperative adjuvant chemotherapy are important treatments in gastric cancer (2-4). Patients with gastric cancer often present with gastrointestinal symptoms that affect food intake and are



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more likely to be malnourished than those with other malignancies (5). Perioperative malnutrition has been reported to be associated with increased postoperative complications, decreased continuation of postoperative chemotherapy, and a poor long-term prognosis (6-11). A preoperative assessment of the degree of malnutrition may improve the prognosis by identifying high-risk patients in advance and implementing appropriate nutritional interventions. Recently, various inflammatory markers and nutritional indicators, such as the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio, prognostic nutritional index, and C-reactive protein-to-albumin ratio, have been demonstrated to be highly useful for predicting surgical complications and the prognosis of various cancers (12-14).

Among these, the Geriatric Nutritional Risk Index (GNRI) was developed by Bouillanne *et al.* as a tool for predicting the risk of complications and death related to the nutritional status of hospitalized elderly patients (15). The GNRI can be calculated from easily obtainable data, such as the height, weight, and serum albumin. Currently, the GNRI is a useful prognostic factor for various types of cancer, including gastric, esophageal, lung, and renal cell carcinoma (6, 16-18).

In the present study, we attempted to clarify the relationship between the GNRI score and the prognosis of gastric cancer patients after curative gastrectomy for all ages.

Patients and Methods

Patients. Patients who underwent curative resection for gastric cancer at Kanagawa Cancer Center between 2013 and 2020 were selected based on their medical records. The patients' eligibility criteria were as follows: 1) pathologically diagnosed gastric adenocarcinoma; 2) underwent gastrectomy between January 2013 and December 2020 and achieved R0 resection; and 3) had clinical stage I-III disease, according to the 15th edition of the General Rules for Gastric Cancer published by the Japanese Gastric Cancer Association.

Surgical procedure and adjuvant treatment. In principle, patients undergo distal or total gastrectomy with lymphadenectomy. D1+ lymph node dissection was performed for clinical T1 and N0 disease, whereas D2 lymph node dissection was performed for clinical T \geq 2 or N \geq 1 disease. Patients diagnosed with pathological stage II or III disease received adjuvant chemotherapy for one year.

Evaluations, statistical analyses, and ethics. The GNRI can be calculated from easily obtainable data such as height, weight, and serum albumin and is calculated using the following formula: $GNRI = [14.89 \times \text{serum albumin (g/dl)}] + [41.7 \times (\text{current body weight (kg)} / \text{ideal weight (kg)})]$; if the current weight/ideal weight was >1 , it was set to 1. The ideal weight for males was $\text{height (cm)} - 100 - [(\text{height (cm)} - 150) / 4]$, and the ideal weight for females was $\text{height (cm)} - 100 - [(\text{height (cm)} - 150) / 2.5]$. The GNRI score classifies the risk of malnutrition into four categories as follows: $GNRI \geq 98$, no risk; $98 > GNRI \geq 92$, mild risk; $92 > GNRI \geq 82$, moderate risk; and $GNRI < 82$, severe risk. The overall survival (OS) was defined as the time from surgery to death, and the recurrence-free survival (RFS) was defined as the time from surgery to recurrence or death. The Kaplan-Meier method was used to calculate the OS and RFS curves. Univariate and multivariate survival analyses were performed using the Cox proportional hazard model. Statistical significance was set at $p < 0.05$. Categorical values are presented as numbers and percentages, while continuous values are represented using median and range values. The chi-square test was used to compare the two groups.

All statistical analyses were performed using EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria). More precisely, it is a modified version of the R commander designed to add statistical functions frequently used in biostatistics. This study was approved by the Institutional Review Board (IRB) of Kanagawa Cancer Center.

Table I. Comparison of the patient background characteristics.

	All patients (%) (n=940)	GNRI ≥98 n=724	GNRI <98 n=216	p-Value
Age (years) (range)	69 (27-90)	68 (32-89)	73 (27-90)	<0.001
Age (years)				
<70	478	398 (55.0)	80 (37.0)	<0.001
≥70	462	326 (45.0)	136 (63.0)	
Sex				
Female	325	230 (31.8)	95 (44.0)	0.001
Male	615	494 (68.2)	121 (56.0)	
Site of tumor				
Upper	212	166 (22.9)	46 (21.3)	0.644
Middle/Lower	728	558 (77.1)	170 (78.7)	
T status				
T1	570	471 (65.1)	99 (45.8)	<0.001
T2 to T3	370	253 (34.9)	117 (54.2)	
Lymph node metastasis				
Negative	651	528 (72.9)	123 (56.9)	<0.001
Positive	289	196 (27.1)	93 (43.1)	
Lymph-vascular invasion				
Negative	449	370 (51.1)	79 (36.6)	<0.001
Positive	491	354 (48.9)	137 (63.4)	
Postoperative surgical complications				
No	704	548 (75.5)	156 (72.2)	0.325
Yes	236	176 (24.3)	60 (27.8)	
Histological type				
Intestinal	468	363 (50.1)	105 (48.6)	0.699
Diffuse	472	361 (49.9)	111 (51.4)	

GNRI: Geriatric Nutritional Risk Index.

Results

Patient characteristics. In total, 940 patients were included in this study. The median patient age was 69 (27-90) years old. Among the 940 patients, 325 (34.6%) were female, and 615 (65.4%) were male. The patients were classified according to the GNRI into a high-GNRI group (GNRI ≥98) and a low-GNRI group (GNRI <98).

There were 724 patients in the high-GNRI group and 216 in the low-GNRI group. Patient backgrounds are shown in Table I. A significantly larger proportion of patients in the high-GNRI group were under 70 years old, and a larger proportion were male than in the low-GNRI group.

Histopathology results showed that T1, N0, and Ly0 were significantly more common in the high-GNRI group than in the low-GNRI group (65.1% vs. 45.8%, $p<0.001$;

72.9% vs. 56.9%, $p<0.001$; 51.1% vs. 36.6%, $p<0.001$). There were no significant differences in tumor location, histological type, or postoperative complication rates between the two groups.

Survival analyses and patterns of recurrence. The respective 3- and 5-year OS rates were 92.0% and 86.3% in the high-GNRI group and 82.4% and 73.2% in the low-GNRI group ($p<0.001$) (Figure 1). In the univariate analysis, age, sex, T-factor, lymph node metastasis, vascular invasion, GNRI, and postoperative complications were related to the OS. In the multivariate analysis, age, sex, T-factor, lymph node metastasis, vascular invasion, and GNRI were independent predictors of the OS (Table II).

The respective 3- and 5-year RFS rates were 89.1% and 84.6% in the high-GNRI group and 75.9% and 69.8% in the low-GNRI group ($p<0.001$) (Figure 2). In the

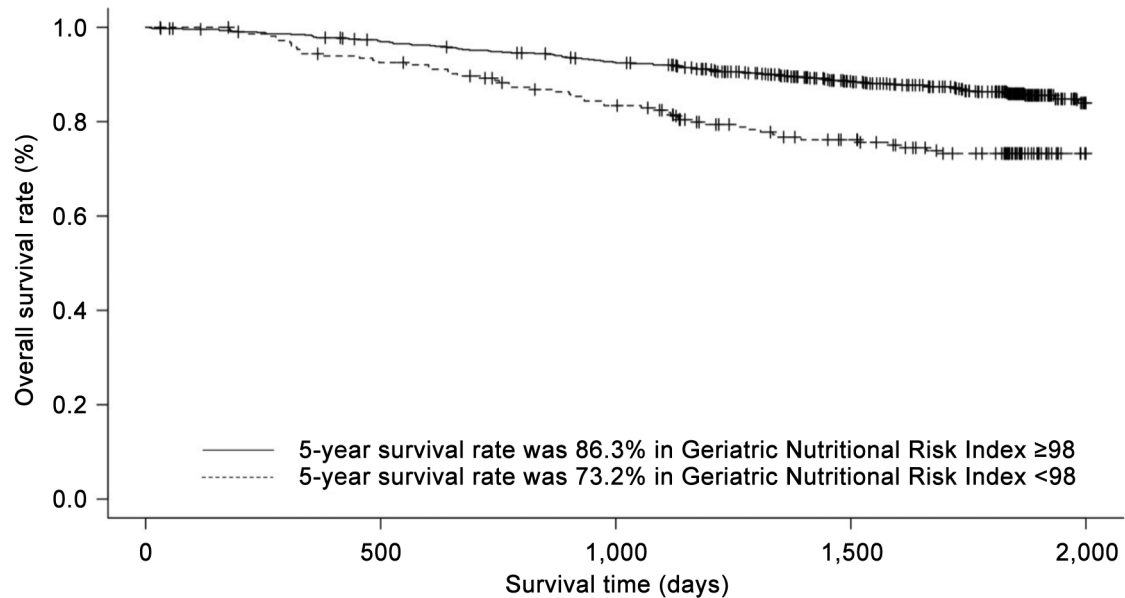


Figure 1. Overall survival of patients with gastric cancer in the Geriatric Nutritional Risk Index (GNRI)-high (≥ 98) and GNRI-low (< 98) groups.

Table II. Uni and multivariate Cox proportional hazards analysis of clinicopathological factors for overall survival.

Factors	No	Univariate analysis			Multivariate analysis		
		OR	95%CI	p-Value	OR	95%CI	p-Value
Age (years)				<0.001			<0.001
<70	478	1.000			1.000		
≥ 70	462	2.523	1.829-3.48		2.020	1.453-2.807	
Sex				<0.001			<0.001
Female	325	1.000			1.000		
Male	462	1.985	1.384-2.846		1.884	1.307-2.714	
T status				<0.001			0.035
T1	570	1.000			1.000		
T2 or more	370	2.884	2.115-3.933		1.509	1.030-2.211	
Lymph node metastasis				<0.001			0.005
Negative	651	1.000			1.000		
Positive	289	2.976	2.201-4.025		1.665	1.170-2.370	
GNRI				<0.001			0.009
≥ 98	724	1.000			1.000		
< 98	216	2.037	1.488-2.79		1.539	1.112-2.132	
Lymph-vascular invasion				<0.001			0.011
Negative	449	1.000			1.000		
Positive	491	3.347			1.729	1.134-2.637	
Tumor location			2.348-4.77	0.065			
Middle, lower	728	1.000					
Upper	212	1.369	0.981-1.912				
Postoperative complications				0.032			0.462
No	704	1.000			1.000		
Yes	236	1.425	1.032-1.967		1.131	0.815-1.568	

GNRI: Geriatric Nutritional Risk Index.

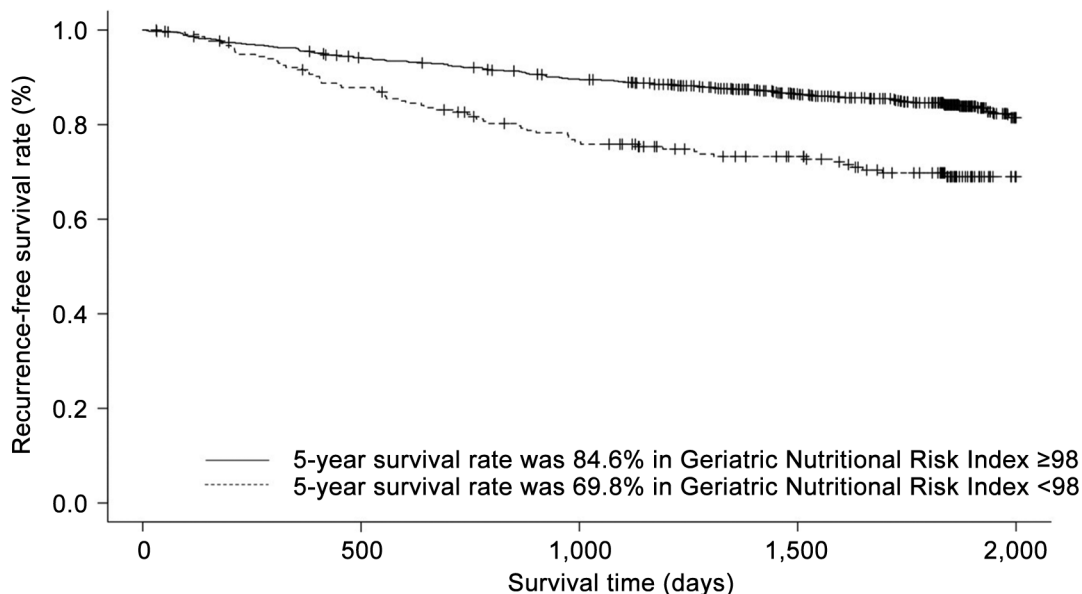


Figure 2. Recurrence-free survival of patients with gastric cancer in the Geriatric Nutritional Risk Index (GNRI)-high (≥ 98) and GNRI-low (< 98) groups.

univariate analysis, age, sex, T-factor, lymph node metastasis, vascular invasion, and GNRI were related to the RFS. In the multivariate analysis, age, sex, lymph node metastasis, vascular invasion, and GNRI were independent predictors of the RFS (Table III).

Regarding the site of first recurrence, hematogenous metastasis was significantly more common in the low-GNRI group (2.6% vs. 6.5%, $p=0.011$), whereas there was no difference in peritoneal dissemination and lymph node recurrence between the two groups (peritoneal dissemination, 3.7% vs. 6.9%, $p=0.059$; lymph node recurrence, 1.8% vs. 4.2%, $p=0.068$) (Table IV).

The postoperative treatment course. There was no marked difference in the incidence of postoperative complications between the high- and low-GNRI groups (24.3% vs. 27.8%, $p=0.325$). The proportion of patients who were eligible for adjuvant chemotherapy was significantly lower in the high-GNRI group (27.2% vs. 45.4%, $p<0.001$), and the proportion of patients who actually received adjuvant chemotherapy did not differ between the two groups (21.0% vs. 27.3%, $p=0.063$).

Discussion

The purpose of this study was to evaluate the impact of the GNRI on the prognosis of patients undergoing radical gastrectomy. Our main finding was that a high GNRI (> 98) was an independent risk factor for the OS and RFS. Furthermore, the need for adjuvant chemotherapy was significantly lower in the high-GNRI group than in the low-GNRI group. This suggests that the GNRI is a useful predictor of the clinical prognosis in patients after curative resection of gastric cancer.

In the present study, the hazard ratio of GNRI to OS was 2.037 [95% confidence interval (CI)=1.488-2.790, $p<0.001$] and that of the GNRI score to RFS was 2.099 (95%CI=1.564-2.817, $p<0.001$). Similar results have been observed previously. Furuke *et al.* classified 795 patients who underwent radical resection for gastric cancer into two groups according to GNRI: high GNRI (≥ 92) and low GNRI (< 92) and investigated short- and long-term outcomes. The 5-year survival rate was 84% for high GNRI and 46% for low GNRI ($p<0.001$). On a multivariate analysis, the OS was significantly lower with a low GNRI

Table III. Uni and multivariate Cox proportional hazards analysis of clinicopathological factors for recurrence-free survival.

Factors	No	Univariate analysis			Multivariate analysis		
		OR	95%CI	p-Value	OR	95%CI	p-Value
Age (years)				<0.001			<0.001
<70	478	1.000			1.000		
≥70	462	2.576	1.903-3.488		2.083	1.530-2.836	
Sex				<0.001			<0.001
Female	325	1.000			1.000		
Male	462	1.998	1.424-2.804		1.953	1.386-2.751	
T status				<0.001			0.128
T1	570	1.000			1.000		
T2 or more	370	2.791	2.09-3.728		1.317	0.924-1.878	
Lymph node metastasis				<0.001			<0.001
Negative	651	1.000			1.000		
Positive	289	3.393	2.553-4.509		2.026	1.451-2.829	
GNRI				<0.001			0.002
≥98	724	1.000			1.000		
<98	216	2.099	1.564-2.817		1.614	1.191-2.188	
Lymph-vascular invasion				<0.001			0.003
Negative	449	1.000			1.000		
Positive	491	3.495	2.504-4.879		1.807	1.221-2.676	
Tumor location				0.054			
Middle, lower	728	1.000					
Upper	212	1.362	0.994-1.865				
Postoperative complications				0.185			
No	704	1.000					
Yes	236	1.234	0.904-1.684				

GNRI: Geriatric Nutritional Risk Index.

than with a high GNRI [hazard ratio (HR)=2.34, 95%CI=1.47-3.64, $p<0.001$]. They concluded that GNRI may be a useful index for assessing short- and long-term outcomes in patients undergoing radical resection for gastric cancer (19).

Matsunaga *et al.* conducted a multicenter study of the GNRI as a prognostic factor in 497 elderly patients ≥75 years old who had undergone radical resection for gastric cancer. The cutoff value was set at 97 by a receiver operating characteristic (ROC) analysis, and patients were classified into the high-GNRI group (≥97) and low-GNRI group (<97). The OS was significantly worse in the low-GNRI group. A multivariate analysis showed that the GNRI was an independent prognostic factor for the OS (HR=1.905, 95%CI=1.374-2.641, $p<0.001$) (20). Hirahara *et al.* studied the long-term survival of 297 patients ≥65 years old who underwent laparoscopic radical resection

Table IV. Patterns of recurrence.

Recurrence site	GNRI ≥98		GNRI <98		p-Value
	Number	%	Number	%	
Peritoneal recurrence	27	3.7	15	6.9	0.059
Hematological recurrence	19	2.6	14	6.5	0.011
Lymph node recurrence	13	1.8	9	4.2	0.068

GNRI: Geriatric Nutritional Risk Index.

for gastric cancer. The cutoff value was set at 94.8 by an ROC analysis, and patients were classified into a high-GNRI group (≥94.8) and a low-GNRI group (<94.8). The 5-year OS rates were 52.2% and 78.9% in the low- and high-GNRI groups, respectively ($p<0.001$). Patients with a low GNRI had a significantly improved prognosis in the stage I group ($p<0.001$) but not in the stage II/III group ($p=0.391$,

$p=0.514$), and a multivariate analysis showed that the GNRI was an independent prognostic factor for the OS (HR=2.35, 95%CI=1.436-3.847, $p<0.001$). They concluded that the GNRI is significantly associated with the OS in elderly gastric cancer patients, is an independent prognostic factor, and is a simple, cost-effective, and promising nutritional indicator (21).

One possible reason the GNRI influences the patient survival involves postoperative complications. Although the GNRI was not a predictor of postoperative complications in the present study, it has been previously reported that the lower the GNRI, the higher the incidence of postoperative complications. Tsutiya *et al.* reported that a low GNRI (<98) was an independent factor associated with postoperative complications (HR=1.97, 95%CI=1.01-3.86, $p=0.047$), but the OS was not identified as a prognostic factor (HR=1.40, 95%CI=0.80-2.44, $p=0.239$) (22). Kushiyama *et al.* investigated whether or not the preoperative GNRI was associated with short-term outcomes in 348 patients ≥ 75 years old who underwent radical resection for gastric cancer. A low GNRI (<98) was an independent predictor of postoperative complications (Clavien-Dindo Classification Grade ≤ 2 ; HR=2.02, 95%CI=1.13-3.66, $p=0.017$). Among the postoperative complications, the incidence of pneumonia was significantly higher in the low-GNRI group than in the high-GNRI group ($p=0.013$). They reported that the preoperative GNRI was a useful indicator of postoperative complications, especially pneumonia (23).

Malnutrition is detrimental to the immune system, is associated with inflammation and cancer cachexia, significantly increases the risk of postoperative complications, increases the side effects of adjuvant chemotherapy, and decreases the efficacy of chemoradiation (24-28). Therefore, assessing the nutritional status of patients is crucial, and biomarkers such as the NLR, Prognostic Nutritional Index (PNI), and CONUT have been developed. However, the gold standard for assessing nutritional risk remains unclear.

Soomin *et al.* investigated the GNRI and PNI as determinants of the OS and disease-free survival (DFS) in 450 patients of all ages who underwent radical gastric

cancer surgery. Both the GNRI and PNI were determinants of the OS and DFS. The effects of the GNRI model on the OS and DFS were similar to those of the PNI model (29). Miyamoto *et al.* evaluated the GNRI and NLR and their usefulness as prognostic indicators in 197 patients ≥ 75 years old who had undergone radical resection for gastric cancer. A multivariate analysis identified the GNRI (HR=0.584, 95%CI=0.356-0.960, $p=0.034$) and NLR (HR=2.470, 95%CI=1.503-4.059, $p<0.001$) as independent prognostic factors for the OS. When the GNRI and NLR were combined as the GNRI-NLR score and examined in the three groups, the GNRI-NLR score was identified as an independent prognostic factor for the OS in multivariate analysis (HR=0.486, 95%CI=0.363-0.651, $p<0.001$). That was the first study to evaluate the prognostic potential of the GNRI-NLR composite index, concluding that the GNRI and NLR are useful prognostic markers in elderly gastric cancer patients and that the GNRI-NLR score may contribute to a more personalized and holistic approach to cancer treatment (30).

Study limitations. First, this was a single-center retrospective study, which may have increased the risk of selection bias, although the number of patients included was higher than that in other studies. Considering the heterogeneity of the population, a large number of cases from multiple centers should be included. Second, we were unable to assess factors (*e.g.*, medications) that might have influenced immunonutritional status prior to surgery. To assess the degree of influence, an interventional study comparing preoperative nutrition with and without intervention is required.

Conclusion

The GNRI is an objective, noninvasive, and readily available biomarker for predicting prognosis in gastric cancer patients and is an independent prognostic factor at all ages after radical resection of gastric cancer. Patient stratification using the GNRI and preoperative nutritional intervention may improve prognosis.

Conflicts of Interest

The Authors have no conflicts of interest to declare in relation to this study.

Authors' Contributions

MT and TA contributed substantially to this concept and design. TA, IH, YM, and TO made substantial contributions to the data acquisition, analysis, and interpretation. TA, IH, YN, JM, KK, SN, YM, YT, TO, AS, and TO were involved in drafting the manuscript and critically revising it for important intellectual content. TA and IH approved the final version of the manuscript.

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