

Original Research Article

## Low Geriatric Nutritional Risk Index (GNRI) Predicts Poorer Survival in Patients with Obstructive Colorectal Cancer Who Had a Self-Expandable Metallic Stent (SEMS) Inserted as a Bridge to Curative Surgery

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### Abstract

**Objectives:** The geriatric nutritional risk index (GNRI) is a nutrition-related risk index calculated easily from serum albumin and the ratio of body weight to ideal body weight. We investigated the prognostic values of the GNRI in elderly patients with obstructive colorectal cancer (OCRC) who had a self-expandable metallic stent inserted as a bridge to curative surgery.

**Methods:** We retrospectively evaluated 61 patients aged  $\geq 65$  years with pathological stage I to III OCRC. Associations of preoperative GNRI and pre-stenting GNRI (ps-GNRI) with short- and long-term outcomes were examined.

**Results:** Multivariate analyses revealed GNRI of  $< 85.3$  and ps-GNRI of  $< 92.9$  were independently associated with worse cancer-specific survival (CSS;  $P = 0.016$ , and  $P = 0.041$ , respectively), and overall survival (OS;  $P = 0.020$ , and  $P = 0.024$ , respectively). A ps-GNRI of  $< 92.9$  was correlated with poorer relapse-free survival (RFS) only in the univariate analysis ( $P = 0.034$ ). For the OCRC cohort without age restriction ( $n = 86$ ), GNRI of  $< 85.3$  and ps-GNRI of  $< 92.9$  were independently associated with worse CSS ( $P = 0.021$ ), and OS ( $P = 0.023$ ), respectively. In univariate analysis, ps-GNRI of  $< 92.9$  was significantly correlated with poorer RFS ( $P = 0.006$ ). Moreover, ps-GNRI of  $< 92.9$  was significantly associated with Clavien-Dindo grade of  $\geq III$  postoperative complications ( $P = 0.037$ ), anastomotic leak ( $P = 0.032$ ), infectious complications ( $P = 0.002$ ), and longer postoperative hospital stay (17 days vs. 15 days;  $P = 0.048$ ).

**Conclusions:** In OCRC patients, decreased preoperative and pre-stenting GNRI were significantly correlated with poorer survival, and decreased pre-stenting GNRI was significantly associated with worse short- and long-term outcomes.

### Keywords

obstruction, colon, Geriatric Nutritional Risk Index, prognosis, cancer

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### Introduction

People older than 65 years comprise up to 28.2% of the total population in Japan, which had the oldest population in

the world as of 2019[1]. Because malignancy inevitably affects the aging population, understanding its impact on the elderly population has become increasingly important. The geriatric nutritional risk index (GNRI) is a nutrition-related

risk index developed by Bouillanne et al. in 2005, and is calculated from serum albumin, body weight, and ideal body weight. The GNRI was found to be correlated with mortality and morbidity in hospitalized elderly patients[2]. With regard to cancer, albumin serves as an antioxidant against carcinogens, suppressing the growth of cancer cell lines, and stabilizing cell growth and DNA replication[3]. Poor cancer survival and immune-suppressed conditions have been linked to hypoalbuminemia[4]. Low body mass index (BMI) and weight loss were correlated with poor cancer survival[5]. Only recently have studies demonstrated that the GNRI predicted prognosis and postoperative complications in elderly patients with malignancy including colorectal cancer (CRC)[6].

CRC ranks second in cancer-related deaths worldwide[7]. Intestinal obstruction is a common presenting symptom of CRC, with an incidence of 10%-20%[8-10]. Moreover, 77% of colonic emergencies are caused by obstructive colorectal cancer (OCRC), which typically requires multiple-stage surgery and is associated with a high rate of morbidity and stoma creation[11]. Endoscopic decompression with a self-expandable metallic colonic stent (SEMS) can convert emergency surgery into elective one-stage surgery, and stenting is considered to be an attractive therapeutic option. Meta-analyses have demonstrated that the long-term outcomes were equivalent to emergency surgery when SEMS was used as a bridge to surgery (BTS)[12,13] or as palliative therapy[14]. In the European Society of Gastrointestinal Endoscopy (ESGE) guideline updated in 2020, placement of a SEMS as a BTS is regarded as a feasible option for emergency resection in patients with potentially curable left-sided obstructing colon cancer[15].

The prognostic significance of GNRI in OCRC patients is unknown. Thus, we evaluated the clinical significance of preoperative and pre-stenting GNRI in elderly patients with non-metastatic OCRC who had a SEMS inserted as a BTS and were subsequently treated with curative surgery.

## Methods

This study retrospectively enrolled patients with non-metastatic OCRC aged 65 years or older who had a SEMS inserted as a BTS between 2013 and 2020. The patients had total or subtotal malignant colonic obstruction and exhibited the following symptoms and findings: (1) obstructive symptoms such as vomiting, abdominal pain, fullness, and constipation; (2) contrast-enhanced computed tomography findings of colorectal tumor with dilation of proximal bowel; and (3) severe stricture or obstruction revealed by contrast enema and colonoscopy. Patients were excluded if there were signs of perforation, peritonitis, or other serious complications necessitating urgent surgery. We excluded patients with benign disease, distant metastasis, positive surgical margin, and in-

vasion from a non-colonic malignancy from the study. No patients had chronic inflammation such as inflammatory bowel disease. None of the patients were treated with neoadjuvant chemoradiation therapy. The study protocol was approved by the ethics committee of the institution with a waiver of informed consent (No. 2019-0008) and conformed to the provisions of the Declaration of Helsinki.

We assessed the degree of obstruction using the ColoRectal Obstruction Scoring System (CROSS), which assigns a point score based on the patient's oral intake level: CROSS 0, requiring continuous decompression; CROSS 1, no oral intake; CROSS 2, liquid or enteral nutrient intake; CROSS 3, soft solids, low-residue, and full diet with symptoms of stricture; and CROSS 4, soft solids, low-residue, and full diet without symptoms of stricture[16]. Endoscopists inserted a SEMS under endoscopic and fluoroscopic guidance. A guidewire was introduced across the malignant stricture, and HANAROSTENT (Boston Scientific, Tokyo, Japan) or Niti-S colonic stent (TaeWoong Medical, Gimpo-si, Korea) was deployed over the wire without balloon dilatation. The colon proximal to the stricture was examined by water-soluble contrast enema or colonoscopy examination.

All patients were subsequently treated with curative surgery. Postoperative complications were classified using the Clavien-Dindo classification[17]. Pathological tumor staging was performed based on the AJCC cancer staging manual (seventh edition)[18]. Colonic lesions proximal to the splenic flexure were defined as right-sided tumors. Long-term outcomes were defined as cancer-specific survival (CSS), overall survival (OS), and relapse-free survival (RFS). CSS was measured from the date of the surgery to the date of death from recurrent cancer, and OS was measured to the date of death from any cause. RFS was measured from the date of the surgery to the date of disease recurrence or death from any cause.

The blood samples were obtained before stenting and surgery. Anemia was defined as hemoglobin of <13 g/dL in males and of <12 g/dL in females[19], and hypoalbuminemia was defined as serum albumin of <3.5 g/dL. The formula of GNRI was  $GNRI = 1.489 \times \text{serum albumin (g/L)} + 41.7 \times \text{body weight (BW)}/\text{ideal body weight (IBW)}$ . We defined ideal body weight in this study as  $IBW = [\text{height (m)}]^2 \times 22$ , which was equal to a BMI of 22 kg/m<sup>2</sup>. When the BW of the patient exceeded the IBW, the BW/IBW was set at 1[20].

Continuous variables were presented as mean  $\pm$  standard deviation (SD) or median (range) and compared using the paired t-test or Mann-Whitney U test, as appropriate. Categorical variables were analyzed in a cross-table using Fisher's exact test. The cutoff value was determined by receiver operating characteristic (ROC) curve analysis using OS as an endpoint. The cutoff value was determined using the most prominent point on the ROC curve (Youden index

**Table 1.** Characteristics of the 61 Elderly Patients with Obstructive Colorectal Cancer.

Value		Value	
Age	75	Harvested lymph node	
[min-max]	[65-93]	<12	5
Gender		≥12	56
Male	35	CROSS before stent placement	
Female	26	0	34
BMI	21.5	1	6
[min-max]	[17.0-28.5]	2	8
ASA-PS		3	13
1	8	Bridging interval (d)	17
2	47	[min-max]	[6-47]
3	6	Type of surgery	
Anemia <sup>a</sup>		Resection with primary anastomosis	54
-	14	Resection with diverting stoma	3
+	47	Hartmann's procedure	4
Hypoalbuminemia <sup>a</sup>		Laparoscopic resection (conversion)	25 (3)
-	12	Postoperative complications <sup>b</sup>	
+	49	Grade I	10
Tumor site		Grade II	10
left	42	Grade III	2
right	19	Grade IV	2
Depth of invasion (T stage)		Grade V	1
T2	1	Anastomotic leak	
T3	45	-	58
T4	15	+	3
Lymph node metastasis (N stage)		Infectious complications	
-	34	-	48
+	27	+	13
Lymphatic invasion		Postoperative hospital stay (d)	16
-	14	[min-max]	[8-77]
+	47	Adjuvant chemotherapy	
Venous invasion		-	36
-	17	+	25
+	44		
Histological differentiation			
tub	60		
por	1		

ASA-PS American Society of Anesthesiologists-Physical Status

CROSS ColoRectal Obstruction Scoring System

<sup>a</sup> Preoperative values.

<sup>b</sup> Clavien-Dindo classification.

= maximum [sensitivity - (1 - specificity)], and the area under the ROC (AUROC) curve was also calculated. Survival curves were generated according to the Kaplan-Meier method and were compared by the log-rank test. Cox proportional hazards model was used for multivariate analyses. Factors with a P-value of <0.1 in the univariate analyses were included in the multivariate model. EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria), was used for statistical analyses, and differences with P values of <0.05 were con-

sidered significant[21].

## Results

Among 92 patients with OCRC who received curative surgery after stenting during the study period, 63 individuals were aged 65 years or older, and GNRI values were available in 61 patients. Table 1 shows the characteristics of the 61 patients. The median age of the patients was 75 years (range, 65-93 years), and the median duration of follow-up was 33 months (range, 1-104 months). There were 35 males

(57.4%) and 26 females. The tumor was located on the left in 42 cases (68.9%) and on the right in 19 cases. The median interval between SEMS insertion and surgery was 17 days (range, 6-47 days). Laparoscopic surgery was performed in 25 (41.0%) cases and 3 cases (12.0%) were converted to open procedure due to severe adhesion. The remaining 36 cases (59.0%) were treated with an open surgical approach. With regard to the CROSS classification, 34 cases (55.7%) were CROSS 0, 6 (9.8%) were CROSS 1, 8 (13.1%) were CROSS 2, and 13 (21.3%) were CROSS 3. As for SEMS insertion, both technical success which was defined as correct placement, and clinical success which was defined as amelioration of occlusive symptoms were 100%. Regarding stenting-related complications, one patient complained of mild abdominal pain after SEMS placement.

Fifty-four patients (88.5%) underwent curative resection with primary anastomosis. Stoma was created in 7 patients including 3 diverting stomas. There were 25 (41.0%) postoperative complications, with 5 (8.2%) major postoperative complications (Clavien-Dindo grade III or greater), including one in-hospital death secondary to anastomotic leakage. The most frequent major and all-grade complications were anastomotic leak ( $n = 3$ ) and ileus ( $n = 8$ ), respectively. Infectious complications were observed in 13 cases, and wound infection was the most frequent infectious complication ( $n = 6$ ). The median postoperative hospital stay was 16 days (range, 8-77 days). Adjuvant chemotherapy was administered in 25 cases (41.0%).

The median interval between blood sampling and surgery was 1 day (range, 0-27 days). The mean ( $\pm$ SD) preoperative GNRI was  $87.1 \pm 7.3$ . ROC curve analysis revealed an optimal cutoff value for preoperative GNRI of 85.3, with a sensitivity of 75%, a specificity of 59%, and an AUROC of 0.64. There were 20 cases (32.8%) in the GNRI of  $<85.3$  group. Table 2 shows the relationship between GNRI status and the clinicopathological parameters of the patients. The GNRI of  $<85.3$  status was significantly associated with advanced age ( $P = 0.018$ ) and anemia ( $P = 0.002$ ). There were no differences between the groups in other clinicopathological factors, including lymphnode metastasis, postoperative hospital stay, and administration of adjuvant chemotherapy.

Kaplan-Meier survival curves showed that GNRI of  $<85.3$  was significantly associated with worse CSS and OS ( $P = 0.005$ , and  $P = 0.007$ , respectively) (Figure 1). The difference in RFS was non-significant according to GNRI status ( $P = 0.18$ ).

We next evaluated the prognostic values of pre-stenting GNRI (ps-GNRI). The median interval between blood sampling and stenting was 0 days (range, 0-1 days). The mean ( $\pm$ SD) of ps-GNRI was  $94.2 \pm 6.9$  which was significantly higher than that of preoperative GNRI ( $P < 0.001$ ). The optimal cutoff value for ps-GNRI was 92.9 which provided a sensitivity of 71%, a specificity of 71%, and an AUROC of

0.68. The ps-GNRI of  $<92.9$  was significantly associated with poorer CSS ( $P = 0.019$ ), OS ( $P = 0.001$ ), and RFS ( $P = 0.034$ ) (Figure 2).

Regarding CSS, the results of the univariate analyses revealed that CA 19-9 of  $\geq 37$  ( $P = 0.029$ ) was a significant adverse prognostic factor (Table S1). The multivariate analysis adjusted for CA19-9 of  $\geq 37$  demonstrated that GNRI of  $<85.3$  [hazard ratio (HR) = 4.32, 95% confidence interval (CI) 1.32-14.22,  $P = 0.016$ ] and ps-GNRI of  $<92.9$  (HR = 3.51, 95% CI 1.05-11.70,  $P = 0.041$ ) were independent negative prognostic factors (Table 3).

Regarding OS, significant poor prognostic factors in the univariate analyses were ASA of  $\geq 3$  ( $P = 0.007$ ), CA 19-9 of  $\geq 37$  ( $P = 0.008$ ), number of the harvested lymph node of  $<12$  ( $P = 0.044$ ), and CD grade of  $\geq$ III complications ( $P = 0.021$ ). In the multivariate analyses, not receiving adjuvant chemotherapy ( $P = 0.069$  in univariate analysis) was included in the model. The result demonstrated that GNRI of  $<85.3$  (HR = 3.67, 95% CI 1.23-10.75,  $P = 0.020$ ) and ps-GNRI of  $<92.9$  (HR = 3.74, 95% CI 1.19-11.75,  $P = 0.024$ ) were independent poor prognostic factors for OS (Table 3). With regard to RFS, ps-GNRI of  $<92.9$  status did not retain a significant prognostic impact in multivariate analysis.

Finally, we evaluated the prognostic values of GNRI in OCRC cases without age restriction. There were 86 OCRC cases whose GNRI values were available. The median age was 71 years (range, 37-93 years), and there were 50 males (58.1%) and 36 females. ROC curve analysis revealed the same cutoff values for preoperative and pre-stenting GNRI. As shown in Table 4, ps-GNRI of  $<92.9$  was significantly associated with anemia ( $P = 0.005$ ), right-sided tumor ( $P = 0.008$ ), CD of  $\geq$ III postoperative complications ( $P = 0.037$ ), anastomotic leak ( $P = 0.032$ ), infectious complications ( $P = 0.002$ ), longer postoperative hospital stay (17 days vs. 15 days;  $P = 0.048$ ), and not administering adjuvant chemotherapy ( $P = 0.021$ ).

Kaplan-Meier survival curves showed significantly worse CSS and OS in the GNRI of  $<85.3$  group ( $P = 0.021$  and  $P = 0.022$ , respectively), while GNRI status did not affect RFS ( $P = 0.08$ ). The ps-GNRI of  $<92.9$  was significantly associated with worse CSS, OS, and RFS ( $P = 0.016$ ,  $P < 0.001$ , and  $P = 0.006$ , respectively) (Figure 3).

Multivariate analyses revealed that GNRI of  $<85.3$  was independently associated with poor CSS (HR = 3.76, 95% CI 1.22-11.61,  $P = 0.021$ ), and ps-GNRI of  $<92.9$  was independently associated with worse OS (HR = 3.68, 95% CI 1.20-11.35,  $P = 0.023$ ) (Table 5).

## Discussion

In the current study, we evaluated the clinical significance of preoperative and pre-stenting GNRI values on short- and long-term outcomes in elderly patients with OCRC who had

**Table 2.** Association between the GNRI Status and the Clinicopathological Parameters in 61 Elderly Patients with Obstructive Colorectal Cancer.

Value	GNRI < 85.3	GNRI ≥ 85.3	P value	ps-GNRI<92.9	ps-GNRI≥92.9	P value
Age	81 [66-93]	74 [65-90]	0.018	75 [65-90]	75 [66-93]	0.93
Gender						
Male	13	22	0.43	14	21	1.00
Female	7	19		10	16	
ASA-PS						
1, 2	17	38	0.38	21	34	0.67
3	3	3		3	3	
CEA (ng/ml) <sup>a</sup>						
<5	8	20	0.78	11	17	1.00
≥5	11	21		13	19	
CA 19-9 (U/ml) <sup>a</sup>						
<37	14	37	0.13	19	32	0.46
≥37	5	4		5	4	
Anemia <sup>b</sup>						
-	0	14	0.002	6	22	0.010
+	20	27		18	15	
CROSS before stent placement						
0	13	21	0.18	13	21	0.64
1	2	4		2	4	
2	0	8		2	6	
3	5	8		7	6	
Bridging interval (d)	17.5 [7-46]	16 [6-47]	0.99	17.5 [7-46]	16 [6-47]	0.54
Tumor site						
left	11	31	0.14	13	29	0.055
right	9	10		11	8	
Depth of invasion (T stage)						
T2, 3	15	31	1.00	19	27	0.76
T4	5	10		5	10	
Lymphnode metastasis (N stage)						
-	14	20	0.17	14	20	0.80
+	6	21		10	17	
Lymphatic invasion						
-	5	9	1.00	6	8	0.77
+	15	32		18	29	
Venous invasion						
-	4	13	0.38	4	13	0.15
+	16	28		20	24	
Histological differentiation						
tub	19	41	0.33	23	37	0.39
por	1	0		1	0	
Harvested lymph node						
<12	2	3	1.00	3	2	0.37
≥12	18	38		21	35	
Complication CD Grade ≥ III						
-	17	39	0.32	20	36	0.073
+	3	2		4	1	
Anastomotic leak						
-	19	39	1.00	21	37	0.056
+	1	2		3	0	

**Table 2.** Association between the GNRI Status and the Clinicopathological Parameters in 61 Elderly Patients with Obstructive Colorectal Cancer (continued).

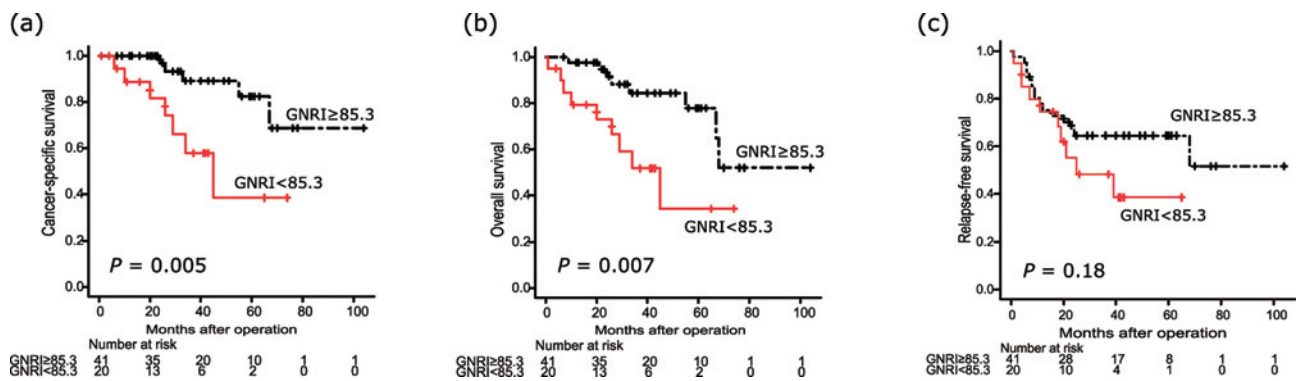
Value	GNRI < 85.3	GNRI ≥ 85.3	P value	ps-GNRI < 92.9	ps-GNRI ≥ 92.9	P value
Infectious complications	14	34	0.32	15	33	0.023
	6	7		9	4	
Postoperative hospital stay (d)	16.5	15	0.20	16.5	15	0.17
	[8-77]	[9-47]		[9-77]	[8-32]	
Adjuvant chemotherapy						
-	14	22	0.28	18	18	0.062
+	6	19		6	19	

CROSS ColoRectal Obstruction Scoring System, CD Clavien-Dindo

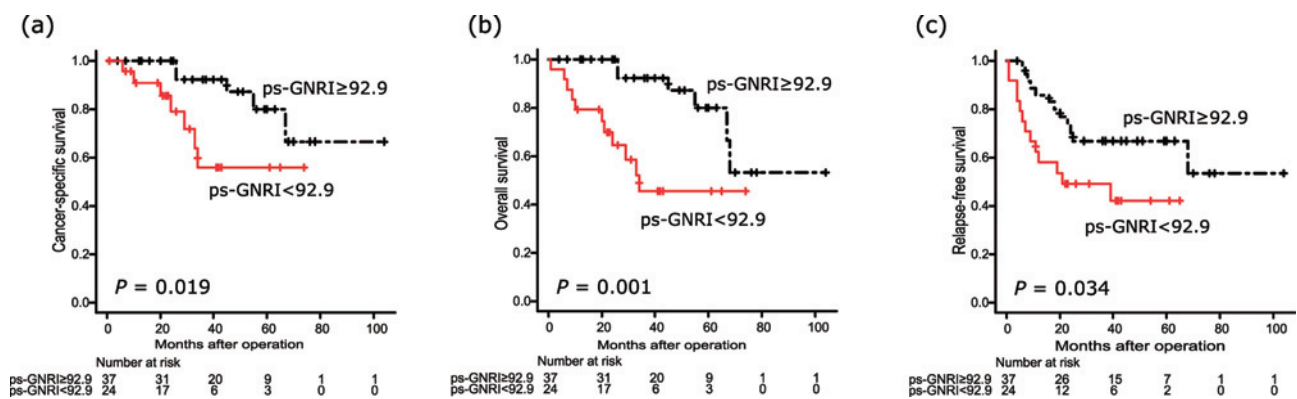
ASA-PS American Society of Anesthesiologists-Physical Status

<sup>a</sup> Data were unavailable in one case.

<sup>b</sup> Evaluated at the corresponding time point.



**Figure 1.** Survival curves of cancer-specific survival (a), overall survival (b), and relapse-free survival (c) of elderly patients with obstructive colorectal cancer based on preoperative GNRI.



**Figure 2.** Survival curves of cancer-specific survival (a), overall survival (b), and relapse-free survival (c) of elderly patients with obstructive colorectal cancer based on pre-stenting GNRI.

a SEMS inserted and underwent curative surgery. The results showed that low preoperative and pre-stenting GNRI were independently associated with poorer CSS and OS. TNM staging is a widely-used, validated staging system for pathological diagnosis and treatment planning. However, the

clinical course of patients in the same stage may differ significantly, highlighting the need for another means of stratification. Molecular parameters, such as BRAF/RAS status and microsatellite instability status, have been demonstrated to function as surrogate markers of drug effectiveness and as

**Table 3.** Multivariate Analysis of Factors Associated with Survival of Elderly Patients with Obstructive Colorectal Cancer.

Value	HR	95% CI	P value
<b>CSS<sup>a</sup></b>			
GNRI (<85.3)	4.32	1.32 - 14.22	0.016
ps-GNRI (<92.9)	3.51	1.05 - 11.70	0.041
<b>OS<sup>b</sup></b>			
GNRI (<85.3)	3.67	1.23 - 10.95	0.020
ps-GNRI (<92.9)	3.74	1.19 - 11.75	0.024
<b>RFS<sup>c</sup></b>			
GNRI (<85.3)	1.92	0.84 - 4.42	0.124
ps-GNRI (<92.9)	1.82	0.75 - 4.46	0.188

<sup>a</sup> Adjusted for CA19-9.

<sup>b</sup> Adjusted for ASA, CA19-9, adjuvant chemotherapy, harvested lymph node <12, and CD Grade  $\geq$  III complications.

<sup>c</sup> Adjusted for ASA, and CA19-9.

CSS cancer-specific survival, OS overall survival, RFS relapse-free survival  
ps-GNRI pre-stenting GNRI

prognostic biomarkers[22,23]. Although they receive much attention and guide the treatment planning for advanced disease[24], these tests as well as TNM staging evaluate tumor characteristics. Accumulating evidence has demonstrated that the nutritional and inflammatory status of the host have significant impacts on the prognosis of cancer. Albumin is the most abundant serum protein that reflects nutritional status. It is also a nonspecific marker of inflammation, chronic disease, and fluid status[25], and hypoalbuminemia is associated with poor cancer survival[4]. Inflammation is regarded as one of the hallmarks of cancer[26]. Inflammation-based markers, such as prognostic nutritional index (PNI), modified Glasgow prognostic score (mGPS), and Controlling Nutritional Status (CONUT) score, are calculated from standard laboratory tests and have been shown to have significant prognostic values in various malignancies including OCRC[27-29]. They are simple and inexpensive to measure, making them easy to apply to everyday practice. GNRI is a simple nutrition-related index calculated from serum albumin, BW, and IBW. It is a modification of the Nutritional Risk Index (NRI) and utilizes a ratio of BW to IBW instead of actual weight loss[2]. Using the ratio has a practical advantage since usual BW, which is defined as stable BW for the past 6 months, is not always available in elderly patients because of impaired memory or lack of records. The index was associated with the prognosis of chronic diseases such as heart failure[30], chronic obstructive pulmonary disease (COPD)[31], and renal failure[32]. As the name suggests, many studies have evaluated GNRI specifically in the elderly population and demonstrated significant prognostic values[2,6,20,31], and this growing body of evidence gives GNRI an advantage over other inflammation-based markers. In recent years, the prognostic significance of GNRI was

demonstrated in multiple malignancies including CRC[20,33-35], colorectal liver metastasis[36], esophageal cancer[37], gastric cancer[38], and hepatocellular carcinoma[39]. In the present study, GNRI of <85.3 and ps-GNRI of <92.9 were independently associated with poorer CSS and OS in elderly patients with OCRC. To the best of our knowledge, this study is the first to demonstrate significant prognostication of GNRI for CSS and OS in patients with OCRC.

The unique preoperative course of patients with OCRC in the BTS setting enables us to evaluate GNRI at two different time points, and preoperative GNRI was significantly lower than pre-stenting GNRI. By placing a SEMS to OCRC cases, emergency surgery with high morbidity and stoma rate can be avoided. The decompression allows for the resumption of a normal diet, medical stabilization with correction of dehydration and electrolyte abnormalities, and the optimization of comorbid illnesses, which theoretically improves a patient's inflammatory and nutritional status. Although both pre-stenting GNRI and preoperative GNRI were significantly associated with long-term outcomes, the change in GNRI values after stenting had no prognostic values (data not shown). On the contrary, we had previously demonstrated that preoperative change in an inflammation-based marker, mGPS, was an independent prognostic factor for OS, using the cohort overlapping with the present one[40]. We had also shown that a bridging interval of 16 days or less might be preferable, because a longer interval was significantly associated with poor short- and long-term outcomes[41]. In the present study, the change in GNRI values after stenting was not associated with the bridging interval (data not shown). These findings suggest that GNRI might not be a good indicator for preoperative dynamic change in nutritional status in the BTS setting. Thus, it might not be appropriate to postpone surgery because of a significant decrease in GNRI value after stenting, and improving the GNRI values might not be a reliable surrogate marker for preoperative medical and nutritional interventions to improve postoperative outcomes. Further work with a larger cohort is needed to investigate the clinical relevance of our findings.

In the OCRC cohort without age restriction, GNRI of <85.3 and ps-GNRI of <92.9 were independent poor prognostic factors for CSS and OS, respectively. GNRI was originally developed to evaluate elderly medical patients without malignancy[2]. Some previous studies demonstrated significant prognostic values of GNRI in patients with cancer in all age groups[33,36,39]. Cancer could pose a significant burden on patients which might be comparable to or even greater than that associated with aging, which could partly explain why GNRI could be prognostic in patients with malignancy without age restriction. In the present study, the ps-GNRI of <92.9 status in the entire cohort was particularly prognostic, and was significantly associated with

**Table 4.** Association between the GNRI Status and the Clinicopathological Parameters in 86 Patients with Obstructive Colorectal Cancer.

Value	GNRI < 85.3	GNRI ≥ 85.3	P value	ps-GNRI<92.9	ps-GNRI≥92.9	P value
Age	74 [44-93]	68.5 [37-90]	0.11	74 [59-90]	69.5 [37-93]	0.071
Gender						
Male	18	32	0.49	16	34	1.00
Female	10	26		12	24	
ASA-PS						
1, 2	25	55	0.39	25	55	0.39
3	3	3		3	3	
CEA (ng/ml) <sup>a</sup>						
<5	13	27	1.00	14	26	0.82
≥5	14	31		14	31	
CA 19-9 (U/ml) <sup>a</sup>						
<37	22	51	0.51	23	50	0.52
≥37	5	7		5	7	
Anemia <sup>b</sup>						
-	27	36	0.0005	21	24	0.005
+	1	22		7	34	
CROSS before stent placement						
0	17	31	0.51	15	33	0.98
1	3	4		2	5	
2	1	8		3	6	
3	7	15		8	14	
Bridging interval (d)	17 [7-46]	16.5 [5-47]	0.69	17.5 [7-46]	16 [5-47]	0.44
Tumor site						
left	17	46	0.076	15	48	0.008
right	11	12		13	10	
Depth of invasion (T stage)						
T2, 3	21	43	1.00	22	42	0.61
T4	7	15		6	16	
Lymphnode metastasis (N stage)						
-	18	26	0.11	16	28	0.50
+	10	32		12	30	
Lymphatic invasion						
-	5	10	1.00	6	9	0.55
+	23	48		22	49	
Venous invasion						
-	6	20	0.32	5	21	0.13
+	22	38		23	37	
Histological differentiation						
tub	27	57	0.55	27	57	0.55
por	1	1		1	1	
Harvested lymph node						
<12	3	3	0.39	4	2	0.085
≥12	25	55		24	56	
Complication CD Grade ≥ III						
-	25	56	0.32	24	57	0.037
+	3	2		4	1	
Anastomotic leak						
-	27	56	1.00	25	58	0.032
+	1	2		3	0	



**Table 4.** Association between the GNRI Status and the Clinicopathological Parameters in 86 Patients with Obstructive Colorectal Cancer (continued).

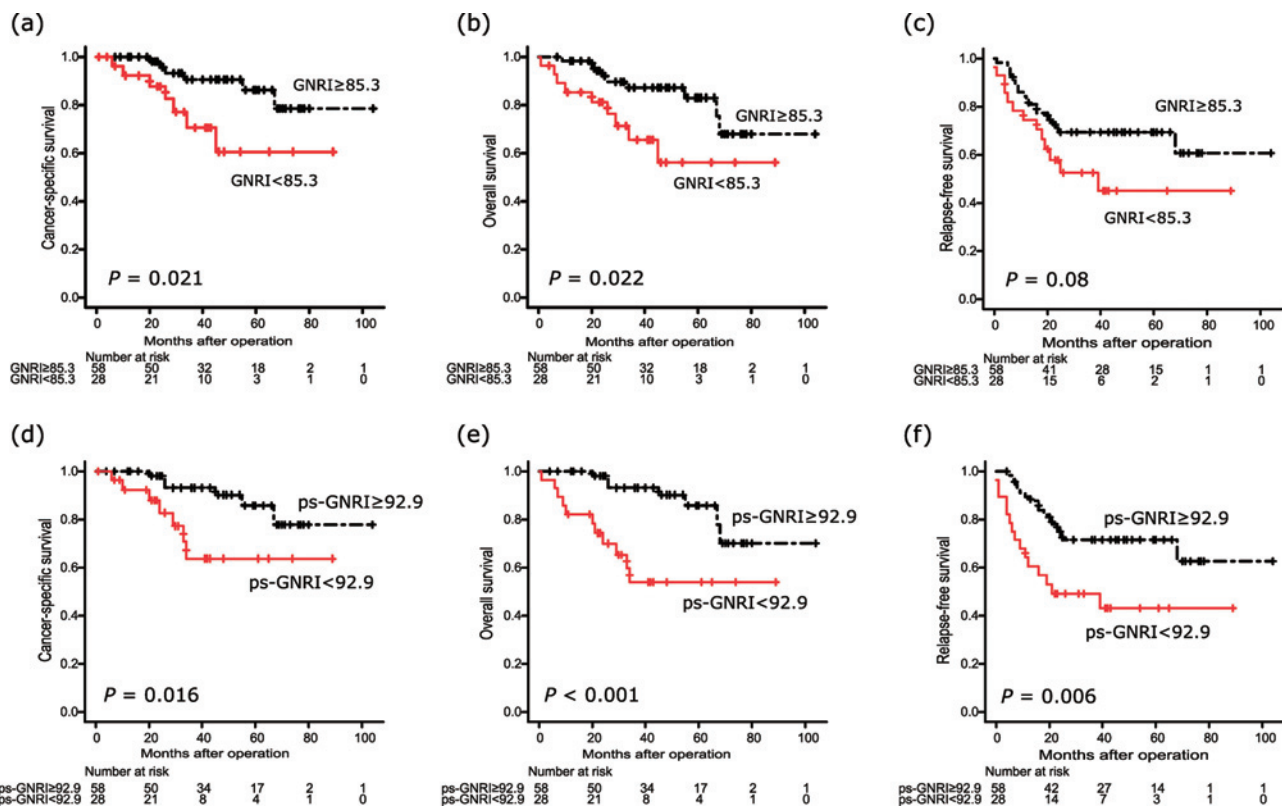
Value	GNRI < 85.3	GNRI ≥ 85.3	P value	ps-GNRI < 92.9	ps-GNRI ≥ 92.9	P value
Infectious complications	20	50	0.14	17	53	0.002
Postoperative hospital stay (d)	8	8		11	5	
	16.5	15.5	0.14	17	15	0.048
	[8-77]	[8-47]		[8-77]	[8-32]	
Adjuvant chemotherapy						
-	16	26	0.36	19	23	0.021
+	12	32		9	35	

CROSS ColoRectal Obstruction Scoring System, CD Clavien-Dindo

ASA-PS American Society of Anesthesiologists-Physical Status

<sup>a</sup> Data were unavailable in one case.

<sup>b</sup> Evaluated at the corresponding time point.



**Figure 3.** Survival curves of cancer-specific survival (a, d), overall survival (b, e), and relapse-free survival (c, f) of patients with obstructive colorectal cancer based on preoperative (a–c) and pre-stenting (d–f) GNRI without age restrictions.

worse long-term outcomes, such as CSS, OS, and RFS, in the univariate analysis. Moreover, it was significantly associated with poorer short-term outcomes, such as CD grade of ≥III postoperative complications, anastomotic leak, and infectious complications. Previous studies demonstrated that a low GNRI was independently associated with CD grade of ≥ II postoperative complications in CRC cases[34,35], and this was the first study to show that GNRI was associated with

anastomotic leak, and infectious complications. These unfavorable short-term outcomes could partly contribute to the longer postoperative hospital stay as well as poorer survival observed in the present study.

This study’s limitations included the limited sample size in a single institution and the retrospective design. In addition, the median follow-up period of 33 months was quite short to conclusively assess the long-term results. The cohort

**Table 5.** Multivariate Analysis of Factors Associated with Survival of Patients with Obstructive Colorectal Cancer.

	Value	HR	95% CI	P value
<b>CSS<sup>a</sup></b>				
GNRI (<85.3)	3.76	1.22	- 11.61	0.021
ps-GNRI (<92.9)	2.80	0.86	- 9.04	0.086
<b>OS<sup>b</sup></b>				
GNRI (<85.3)	2.84	0.98	- 8.27	0.055
ps-GNRI (<92.9)	3.68	1.20	- 11.35	0.023
<b>RFS<sup>c</sup></b>				
GNRI (<85.3)	2.04	0.98	- 4.24	0.057
ps-GNRI (<92.9)	2.05	0.92	- 4.58	0.078

<sup>a</sup> Adjusted for CA19-9, and adjuvant chemotherapy.

<sup>b</sup> Adjusted for age≥70, ASA, CA19-9, adjuvant chemotherapy, harvested lymph node<12, and CD Grade ≥ III complications.

<sup>c</sup> Adjusted for ASA, CA19-9, adjuvant chemotherapy, and CD Grade ≥ III complications.

CSS cancer-specific survival, OS overall survival, RFS relapse-free survival ps-GNRI pre-stenting GNRI

consisted only of patients with OCRC who received curative surgery after having a SEMS placed. They were a distinct group of CRC patients, and thus care must be taken when interpreting our findings.

In summary, the results of the present study demonstrated that preoperative and pre-stenting GNRI were significant predictors of CSS and OS in elderly patients with OCRC. When evaluated without age restriction, pre-stenting GNRI was significantly associated with poorer short- and long-term outcomes. The results implied that in evaluating patients with OCRC, nutritious status represented by GNRI values might be as important as pathological staging. Because GNRI can be easily calculated, it can be readily used in daily clinical practice. Future studies are warranted to validate the results and further elucidate underlying mechanisms.

**Conflicts of Interest**

There are no conflicts of interest.

**Author Contributions**

All listed authors participated meaningfully and met the 4 authorship criteria recommended by ICMJE. They have seen and approved the final manuscript.

**Approval by Institutional Review Board (IRB)**

#2019-0008, Sendai City Medical Center Sendai Open Hospital

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### Supplementary Files

#### Table S1.

#### Table S2.

Please find supplementary file(s);

<http://dx.doi.org/10.23922/jarc.2022-053>

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