

Original Research Article

## Prognostic Significance of Preoperative Globulin-to-albumin Ratio in Obstructive Colorectal Cancer Patients Who Underwent Curative Surgery after Stenting

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### Abstract

**Objectives:** It has been increasingly recognized that the progression of cancer is dependent not only on the tumor characteristics but also on the nutritious and inflammatory condition of the host. We investigated the relationship between the globulin-to-albumin ratio (GAR) and long-term outcomes in obstructive colorectal cancer (OCRC) patients who were inserted self-expandable metallic stent as a bridge to curative surgery.

**Methods:** A total of 75 pathological stage II and III OCRC patients between 2013 and 2020 were retrospectively evaluated. The associations of the preoperative GAR with clinicopathological factors and patient survival were examined.

**Results:** Receiver operating characteristic curve analysis demonstrated that the optimal cutoff value was 0.88. The GAR  $\geq$  0.88 status was significantly associated with the absence of lymph node metastasis (P = 0.011), longer postoperative hospital stay (17 days vs 15 days, P = 0.042), and not receiving adjuvant chemotherapy (P = 0.011). Relapse-free survival and cancer-specific survival were significantly shorter in the GAR  $\geq$  0.88 group (P = 0.007 and P = 0.023, respectively). Multivariate analyses revealed that the GAR  $\geq$  0.88 was independently associated with relapse-free survival [hazard ratio (HR) = 4.17, 95% confidence interval (CI) 1.32-13.14, P = 0.015]. Moreover, CA19-9  $\geq$  37 (HR = 6.56, 95% CI 2.12-20.27, p = 0.001) and not receiving adjuvant chemotherapy (HR = 4.41, 95% CI 1.28-15.26, p = 0.019) were independent poor prognostic factors for relapse-free survival.

**Conclusions:** The results demonstrated that the GAR was a significant prognostic factor for OCRC patients.

### Keywords

cancer, colon, colorectal, globulin-to-albumin ratio, obstruction, self-expandable metallic stent

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### Introduction

Colorectal cancer (CRC) is one of the most frequent cancers in the world. In 2018, an estimated 1.8 million new cases were diagnosed and nearly 880,000 patients died of the disease[1]. CRC often present with obstruction whose

incidence was reaching 30%[2]. Obstructive colorectal cancer (OCRC) constituted 85% of colonic emergency that sometimes required multiple-stage surgery[3]. Recently, intestinal decompression using self-expandable metallic colonic stent (SEMS) as “a bridge to surgery (BTS)” has become an appealing option[4,5]. The decompression allows

bowel preparation, correction of dehydration and electrolyte abnormalities, and optimization of comorbid illnesses, which theoretically improves patients' nutritious and inflammatory conditions. Thus, the patients could be managed by elective one-stage surgery with reduced morbidity and stoma rate compared to emergency surgery[5-7]. SEMS was originally used with palliative intent[8] due to concerns for short-term complications and long-term survival, but recently, it has been increasingly used as a bridge to curative surgery[5-7].

The TNM staging system is a validated staging system that is widely used in diagnostic evaluation and treatment planning. However, the clinical course might vary considerably among the patients in the same stage, highlighting the need for another means for stratification. Molecular parameters, such as the microsatellite instability status and BRAF/RAS status, have been shown to serve as surrogate markers of drug efficacy and as prognostic biomarkers[9,10]. Although they receive substantial attention and guide the treatment planning for advanced disease[11], the tests are expensive and not routinely assessed for every patient. Inflammation-based markers are calculated from standard laboratory results and have been shown to serve as prognostic markers in various malignancies[12]. They are simple and easy to measure without extra cost, which facilitates implantation into daily practice. Globulin-to-albumin ratio (GAR) is one of such markers, and its significant prognostic value was demonstrated in CRC patients who underwent surgery[13-15] and those administered chemotherapy for unresectable disease[16]. However, the prognostic significance of the GAR in OCRC patients was unknown. In this study, we investigated the relationship between the GAR and long-term outcomes in OCRC patients who were inserted a SEMS and subsequently received curative surgery.

## Methods

### Patients

We retrospectively studied consecutive pathological stage II and III OCRC patients who were inserted a SEMS as BTS at Sendai City Medical Center between 2013 and 2020. The patients presented with total or subtotal malignant colonic obstruction characterized by the following symptoms and findings: (1) obstructive symptoms such as abdominal pain, fullness, vomiting, and constipation; (2) contrast-enhanced CT findings of colorectal tumor with dilation of proximal bowel; and (3) severe stricture or obstruction demonstrated by contrast enema and colonoscopy. Patients were excluded if there were signs of peritonitis, perforation, or other serious complications demanding urgent surgery. Patients with benign disease, distant metastasis, positive surgical margin, and invasion from a non-colonic malignancy were excluded from the study. There were no patients with

chronic inflammation. None of the patients received neoadjuvant chemoradiation therapy.

ColoRectal Obstruction Scoring System (CROSS) was used to rate the severity of obstruction. A point score was assigned 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[17].

The SEMS was placed by endoscopists. A guidewire was passed through the malignant stenosis under endoscopic and fluoroscopic guidance. Niti-S colonic stent (TaeWoong Medical, Gimpo-si, Korea) or HANAROSTENT (Boston Scientific, Tokyo, Japan) was deployed over the wire and through the scope without balloon dilatation. The colon proximal to the stricture was evaluated by water-soluble contrast enema, and colonoscopic examination was performed after the surgery.

All patients subsequently underwent curative surgical resection. Postoperative complications were graded with the Clavien-Dindo classification[18]. The tumor was staged according to the AJCC 7th edition cancer staging manual[19]. Colonic lesions proximal to the splenic flexure were defined as right-sided tumors.

The protocol for this research project was approved by the ethics committee of the institution with a waiver of informed consent (#2019-0008), and it conforms to the provisions of the Declaration of Helsinki.

### Statistical analysis

The primary endpoint of the study was long-term outcomes, which were defined as relapse-free survival (RFS) and cancer-specific survival (CSS). RFS was measured from the date of the surgery to the date of the disease recurrence, and CSS was measured from the date of the surgery to the date of death from the recurrent cancer.

The blood samples were collected before stenting and before surgery, and the GAR was calculated using the following formula:  $\text{serum} \left[ \frac{(\text{total protein} - \text{albumin})}{\text{albumin}} \right]$ . Continuous variables were shown as mean and SD or median and range and were tested using the t-test or Mann-Whitney U test, as appropriate. Associations between the GAR and clinicopathological parameters were examined in a cross-table using Fisher's exact test. The cutoff values were established using receiver operating characteristic (ROC) curve analyses using recurrence as an endpoint. The cutoff value was defined using the most prominent point on the ROC curve (Youden index = maximum [sensitivity-(1-specificity)]), and the area under the ROC (AUROC) curve was also calculated. Survival curves were plotted according to the Kaplan-Meier method and were analyzed by the log-rank test. Multivariate analysis was performed using Cox

**Table 1.** Characteristics of the 75 Colorectal Cancer Cases.

Value		Value	
Age	72	CROSS before stent placement	
[min-max]	[37-93]	0	44
Gender		1	7
Male	43	2	8
Female	32	3	16
ASA-PS		Stenting-related complications	2
1, 2	69	Resume normal diet after stenting	51
3	6	Interval between stenting and operation	16
Tumor site		[min-max]	[5-46]
left	54	Type of surgery	
right	21	Resection with primary anastomosis	66
Depth of invasion (T stage)		Resection with diverting stoma	4
T3	56	Hartmann's procedure	5
T4	19	Laparoscopic resection (conversion)	29 (4)
Lymph node metastasis		Postoperative complications <sup>a</sup>	
-	38	Grade I	12
+	37	Grade II	10
Lymphatic invasion		Grade III	3
-	13	Grade IV	1
+	62	Grade V	1
Venous invasion		Postoperative hospital stay (d)	16
-	23	[min-max]	[8-77]
+	52	Adjuvant chemotherapy	
Histological differentiation		-	38
tub	73	+	37
por	2		
Harvested lymph node			
<12	5		
≥12	70		

<sup>a</sup> Clavien-Dindo classification

CROSS ColoRectal Obstruction Scoring System

ASA-PS American Society of Anesthesiologists-Physical Status

proportional hazards model. Factors shown to have a P-value of < 0.1 in the univariate analysis were included in the analysis.

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)[20], and differences with P values < 0.05 were considered significant.

### Results

During the study period, there were 79 pathological stage II and III OCRC cases who had a SEMS placed and received curative surgery. A total of 75 cases were deemed eligible in the present study as all the necessary preoperative data were available for calculating the GAR. Table 1 showed the characteristics of the 75 patients. There were 43 men and 32 women. The median age of the patients was 72 years (range, 37-93), and the median follow-up time was 29

months (range, 1-89). Concerning the CROSS classification, 44 patients (58.7%) were CROSS 0, 7 (9.3%) were CROSS 1, 8 (10.7%) were CROSS 2, and 16 (21.3%) were CROSS 3. The median interval between SEMS insertion and the surgery was 18.0 days (range, 5-46), and the median postoperative hospital stay was 16 days (range, 8-77). Some patients were only allowed a liquid diet after SEMS placement at the discretion of the physician, and 51 patients (68.0%) could resume a normal diet after the decompression. Patients were administered parenteral nutrition to meet the nutritious requirements when necessary.

As for SEMS insertion, the technical success that was defined as correct placement was 100%, and clinical success that was defined as resolution of occlusive symptoms was 97.3%. There were two stenting-related complications. One patient complained of mild abdominal pain after SEMS placement and another patient with inadequate drainage necessitate insertion of a transanal decompression tube for additional drainage.

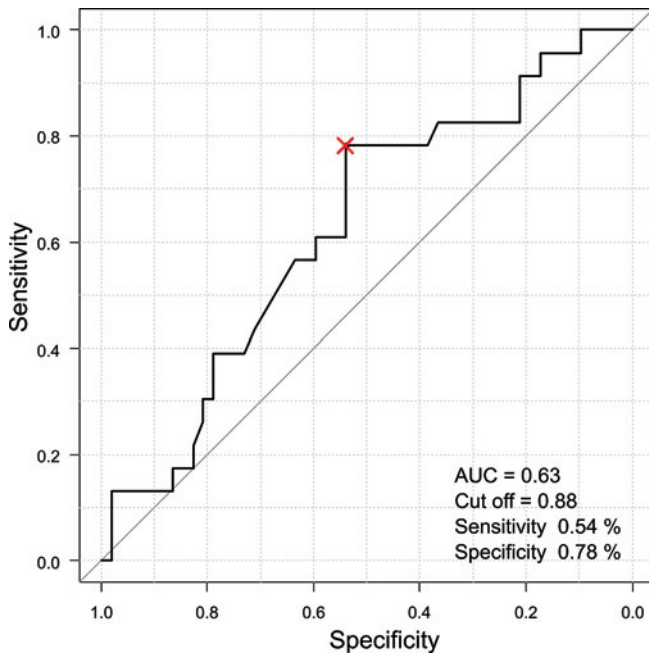
Curative resection with primary anastomosis was achieved in 66 patients (88.0%). Stoma was constructed in nine cases including four diverting stomas. Twenty-nine patients underwent laparoscopic surgery, and conversion to open procedure was required in four cases due to the severe adhesion in three and the tumor with direct invasion to the bladder in one. There were five major postoperative complications that were Clavien-Dindo grade 3 or greater, including one in-hospital death secondary to anastomotic leakage. Adjuvant chemotherapy was administered for 37 cases (49.3%). The

reasons for not administering the chemotherapy were advanced age in 19 (50.0%) followed by patients' preference in 7 (18.4%).

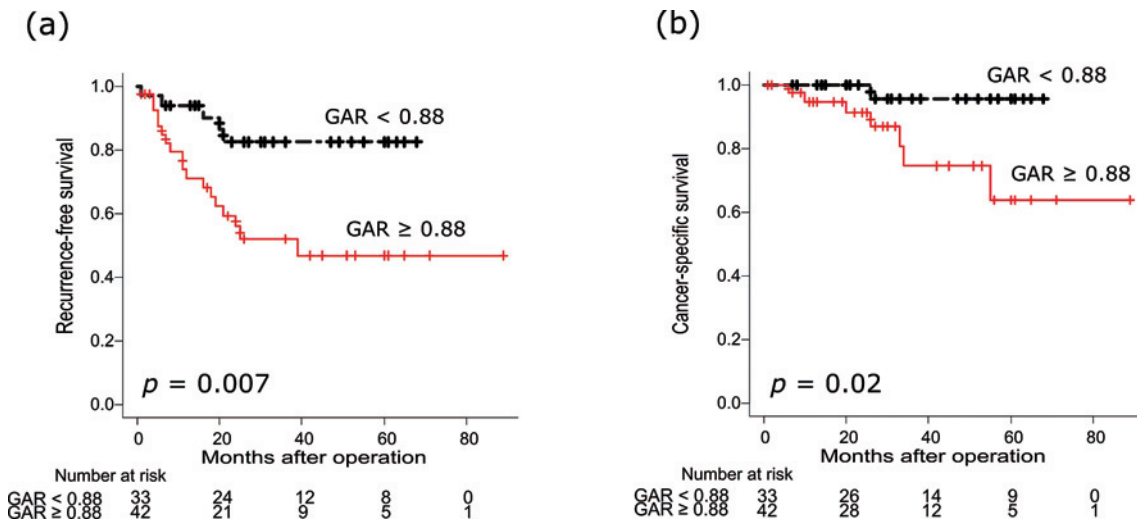
The blood samples were collected before stenting and before surgery. The median interval between blood sampling and surgery was 1 day (range, 1-21). The mean values of pre-stenting and preoperative GAR were  $0.89 \pm 0.22$  and  $0.98 \pm 0.26$ , respectively, and preoperative GAR was significantly higher ( $P < 0.001$ ). For pre-stenting GAR, ROC curve analysis revealed that the optimal cutoff value was 0.88, which provided a sensitivity of 65%, a specificity of 61%, and AUROC of 0.59. For preoperative GAR, the optimal cutoff value was 0.88, with a sensitivity of 54%, a specificity of 78%, and AUROC of 0.63 (Figure 1). As preoperative GAR had higher AUROC, we employed preoperative GAR for subsequent survival analyses.

Kaplan-Meier survival curves demonstrated that RFS and CSS were significantly shorter in the preoperative GAR  $\geq 0.88$  group ( $P = 0.007$  and  $P = 0.023$ , respectively; Figure 2). The relationship between the GAR status and clinicopathological parameters of the 75 patients was shown in Table 2. The GAR  $\geq 0.88$  status was significantly associated with the absence of lymph node metastasis ( $P = 0.011$ ), longer postoperative hospital stay (17 days vs 15 days,  $P = 0.042$ ), and not receiving adjuvant chemotherapy ( $P = 0.011$ ). Other clinicopathological factors and the interval between the SEMS insertion and the surgery were comparable between the groups. Postoperative complications and recurrence patterns were not different regardless of the GAR status.

Adjuvant chemotherapy significantly improved RFS and CSS ( $P = 0.015$  and  $P = 0.011$ , respectively). Patients aged 70 years or older ( $P = 0.0002$ ), ASA score 3 ( $P = 0.025$ ), and absence lymph node metastases ( $P = 0.011$ ) were sig-



**Figure 1.** Receiver operating characteristic curves for the GAR. X indicates the most prominent point.



**Figure 2.** Survival curves of 75 pathological stage II and III obstructive colorectal cancer patients underwent stenting as a bridge to curative surgery. Relapse-free survival (a) and cancer-specific survival (b) were significantly shorter in the GAR  $\geq 0.88$  group.

**Table 2.** Association between the GAR Status and Clinicopathological Parameters in 75 Colorectal Cancer Cases.

Value	GAR		P value	Value	GAR		P value
	<0.88	≥0.88			<0.88	≥0.88	
Age				Histological differentiation			
<70	19	15	0.07	tub	32	41	1.00
≥70	14	27		por	1	1	
Gender				Harvested lymph node			
Male	18	25	0.81	<12	0	5	0.06
Female	15	17		≥12	33	37	
ASA-PS				CROSS before stent placement			
1, 2	32	37	0.22	0	16	28	0.46
3	1	5		1	4	3	
CEA				2	4	4	
<5	15	22	0.64	3	9	7	
≥5	18	19		Interval between stenting and operation (d)			
CA 19-9					16	15.5	0.61
<37	30	35	0.72		[7-43]	[5-46]	
≥37	3	6		Postoperative hospital stay (d)			
Tumor site					15	17	0.042
left	26	28	0.31		[9-47]	[8-77]	
right	7	14		Complication CD Grade ≥ III			
Depth of invasion (T stage)				-	32	38	0.38
T3	24	32	0.79	+	1	4	
T4	9	10		Adjuvant chemotherapy			
Lymph node metastasis (N stage)				-	11	27	0.011
-	11	27	0.011	+	22	15	
+	22	15		Recurrence pattern			
Lymphatic invasion				Lung	1	4	1.00
-	3	10	0.13	Liver	4	8	
+	30	32		Local	0	3	
Venous invasion				Lymph node	0	1	
-	11	12	0.80	Peritoneal dissemination	0	1	
+	22	30					

CROSS ColoRectal Obstruction Scoring System, CD Clavien-Dindo  
 ASA-PS American Society of Anesthesiologists-Physical Status

nificantly associated with not receiving the adjuvant chemotherapy (Table 3). When the patients were stratified according to the regimens of the chemotherapy, those who were administered oxaliplatin-containing regimens (n = 9) were free from recurrence and exhibited better RFS (P = 0.028) and CSS (P = 0.039) in the present study (Figure 3).

With regard to RFS, univariate analyses revealed the GAR ≥ 0.88 (P = 0.012), CA19-9 ≥ 37 (P = 0.002), and not receiving adjuvant chemotherapy (P = 0.021) to be significant prognostic factors. In the multivariate analyses, T stage, N stage, age, and ASA score were included in the model as the potential confounding variables. The result showed that the GAR ≥ 0.88 [hazard ratio (HR) = 4.17, 95% confidence interval (CI) 1.32-13.14, P = 0.015], CA19-9 ≥ 37 (HR = 6.56, 95% CI 2.12-20.27, p = 0.001), and not receiving adjuvant chemotherapy (HR = 4.41, 95% CI 1.28-15.26, p = 0.019) were independent poor prognostic factors (Table 4).

With regard to CSS, no variables were identified as an independent poor prognostic factor in multivariate analysis.

### Discussion

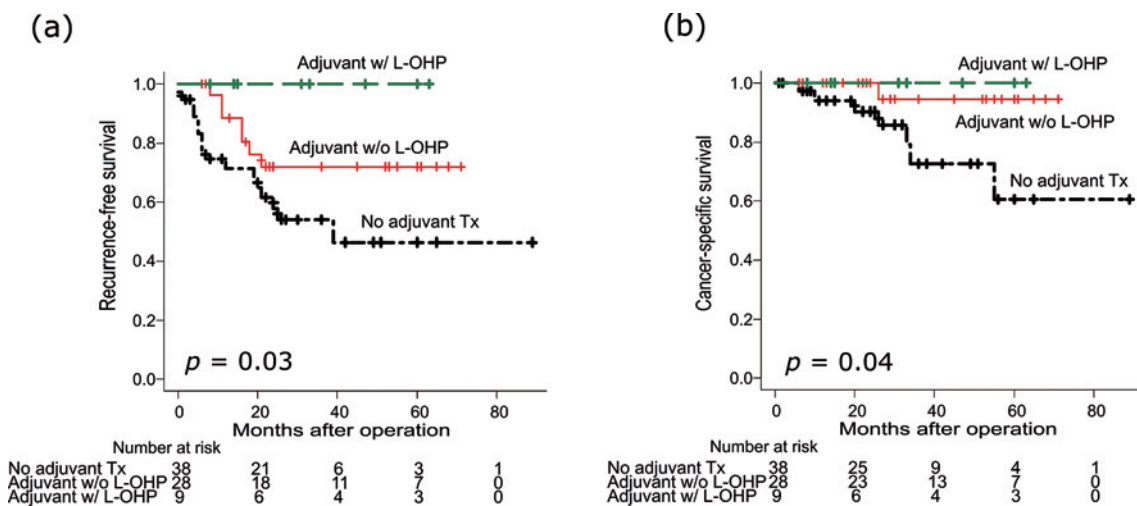
It has been increasingly recognized that the progression of cancer is dependent not only on the tumor characteristics but also on the systemic inflammatory response and nutritious status of the host[12,21,22]. In this study, we investigated the relationship between the GAR and long-term outcomes in stage II and III OCRC patients who had a SEMS placed and underwent curative surgery and demonstrated that the preoperative GAR ≥ 0.88 group had significantly shorter RFS and CSS. Furthermore, the preoperative GAR status was an independent prognostic factor for RFS in multivariate analysis. The GAR was demonstrated to be a strong predictor of survival in various malignancies such as non-small-



**Table 3.** Association between Adjuvant Chemotherapy and Clinicopathological Parameters in 75 Colorectal Cancer Cases.

Value	Adjuvant Tx		P value	Value	Adjuvant Tx		P value
	-	+			-	+	
Age				Lymphatic invasion			
<70	9	25	0.0002	-	9	4	0.22
≥70	29	12		+	29	33	
Gender				Venous invasion			
Male	23	20	0.64	-	11	12	0.81
Female	15	17		+	27	25	
ASA-PS				Histological differentiation			
1, 2	32	37	0.025	tub	37	36	1.00
3	6	0		por	1	1	
CEA				Harvested lymph node			
<5	19	18	1.00	<12	1	4	0.36
≥5	19	18		≥12	36	34	
CA 19-9				Interval between stenting and operation (d)			
<37	33	32	1.00	[5-46]	17	14	0.28
≥37	5	4		[6-43]			
Tumor site				Postoperative hospital stay (d)			
left	25	29	0.31	[8-77]	17	15	0.12
right	13	8		[9-46]			
Depth of invasion (T stage)				Complication CD Grade ≥ III			
T3	28	28	1.00	-	35	35	1.00
T4	10	9		+	3	2	
Lymph node metastasis (N stage)							
-	25	13	0.011				
+	13	24					

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**Figure 3.** Survival curves of 75 pathological stage II and III obstructive colorectal cancer patients underwent stenting as a bridge to curative surgery. Adjuvant chemotherapy significantly improved relapse-free survival (a) and cancer-specific survival (b), and those who were administered oxaliplatin (L-OHP)-containing regimens were free from recurrence.

**Table 4.** Univariate and Multivariate Analysis of Disease-Free Survival in 75 Obstructive Colorectal Cancer Patients.

Variable	Univariate analysis			Multivariate analysis		
	HR	95% CI	P value	HR	95% CI	P value
Gender (male)	1.29	0.56-2.99	0.55			
Age (≥70)	1.43	0.62-3.31	0.40	0.68	0.25-1.87	0.46
ASA-PS (≥3)	2.42	0.71-8.31	0.16	0.49	0.09-2.58	0.40
CEA (≥5)	1.22	0.53-2.78	0.64			
CA 19-9 (≥37)	4.37	1.71-11.18	0.002	6.56	2.12-20.27	0.001
Tumor site (right)	0.96	0.38-2.43	0.92			
Depth of invasion (T4)	2.18	0.94-5.05	0.07	2.04	0.73-5.70	0.17
Lymph node metastasis (N+)	1.67	0.72-3.86	0.23	2.28	0.76-6.88	0.14
Lymphatic invasion (LY+)	0.82	0.28-2.42	0.72			
Venous invasion (V+)	1.19	0.49-2.91	0.70			
Harvested lymph node (<12)	1.53	0.36-6.55	0.56			
Adjuvant chemotherapy (no)	2.85	1.17-6.95	0.021	4.41	1.28-15.26	0.019
GAR (≥0.88)	3.57	1.32-9.63	0.012	4.17	1.32-13.14	0.015

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cell lung cancer[23], urothelial cancer[24], gastric cancer[25], colon cancer[13-16], breast cancer[26], and lymphoma[27]. Interestingly, the predictive value of the GAR was not restricted to malignancies, and the GAR was associated with all-cause mortality after non-ST (electrocardiogram S and T wave interval) elevation myocardial infarction[28], heart failure[29], and autoimmune disease[30]. Moreover, the GAR was associated with all-cause mortality, cancer mortality, and cancer incidence in a general healthy population[31]. The underlying mechanisms for these findings remain elusive. Albumin is the most abundant serum protein that reflects nutritional status, and it is also a non-specific marker of inflammation, chronic disease, and fluid status[32]. Albumin is an antioxidant against carcinogens, suppressing the growth of cancer cell lines and stabilizing cell growth and DNA replication[33]. Hypoalbuminemia was associated with the immune-suppressed condition and poor cancer survival[22]. Globulin comprises carrier proteins, immunoglobulins, complement factors, and enzymes. It includes acute-phase proteins such as C-reactive protein, serum amyloid, α-1-acid glycoprotein, and α-1-antichymotrypsin and reflects immunity and inflammation[34]. Thus, albumin and globulin could be potent indicators of the nutrition, inflammation, and immune status of the host. Since GAR is a ratio of the two, it is less affected by blood constituents, such as dehydration and fluid retention. The GAR was associated with long-term oncological outcomes in colorectal cancer patients who underwent surgery[13-15] and those with unresectable metastatic disease[16]. To the best of our knowledge, this study was the first to reveal the prognostic significance of the GAR in OCRC patients.

The GAR ≥ 0.88 status was significantly associated with

poor prognosis, whereas the status was significantly associated with the absence of lymph node metastasis. Ishibe et al.[35] reported that lymph node involvement did not have a significant impact on disease-free survival (DFS) and CSS in the study of 234 OCRC patients. Similarly, as shown in Table 4, the prognostic value of lymph node metastasis was non-significant in this study, which could partly explain the peculiar relationship between GAR status and N stage. In the previous studies of CRC, the GAR status was significantly associated with age, tumor location, T stage, lymphatic invasion, venous invasion, CEA, and CA 19-9[13,15]. In this study, the GAR ≥ 0.88 status was associated with the absence of lymph node metastasis, longer postoperative hospital stay, and not receiving adjuvant chemotherapy. The discrepancy might suggest that the OCRC patients in the BTS setting possess unique characteristics, which underscore the importance of evaluating the systemic inflammatory response and nutritious status represented by the GAR.

In our previous study using the overlapping OCRC cohort, the preoperative value of the modified Glasgow prognostic score (mGPS) was significantly associated with poor overall survival (OS). Moreover, preoperative change of the mGPS after stenting was significantly associated with the OS and CSS[36]. In this study, GAR was evaluated before stenting and before surgery, and preoperative GAR was significantly higher than pre-stenting GAR. Preoperative GAR had prognostic value, but pre-stenting GAR and preoperative change of the GAR after stenting were not associated with long-term survival. These results suggest that preoperative immuno-nutritious status might have a significant effect on long-term survival of OCRC patients. GAR might not be suitable to evaluate the change of the immuno-nutritious condition since it is a ratio and not necessarily related to ab-

solute values. Still, improvement of the immuno-nutritious status might have a positive impact on survival, which warrants further study.

In this study, preoperative GAR was independent prognostic factor for RFS but not for CSS in multivariate analyses, and AUROC of 0.63 was not very high. One way of improving the discriminative ability is adding factors and constructing nomograms. Li et al.[15] studied 5336 colorectal cancer patients and established nomograms on OS and DFS, and GAR was one of the factors included in their nomograms. Our cohort was too small to generate and validate reliable original nomograms. Study with larger sample size from multiple institutions might be warranted.

Inserting SEMS has raised concerns about short-term complications and long-term survival as it mechanically dilates malignant stricture. SEMS placement was shown to increase viable circulating tumor cells[37], cytokeratin 20 mRNA[38], cell-free DNA, and circulating tumor DNA levels in peripheral blood[39]. SEMS was also associated with perineural invasion[40,41]. However, these worrisome findings might not result in poor prognosis, and meta-analyses revealed that long-term outcomes of SEMS were comparable to emergency surgery when used as a BTS[5-7] and as palliative therapy[42]. Moreover, the incidence of local and distant recurrence was not significantly different[3,5]. When compared with patients treated with a transanal decompression tube, no statistically significant differences were found concerning recurrence patterns and long-term survival[43]. In the 2014 guideline of the European Society of Gastrointestinal Endoscopy, SEMS placement as a BTS was not recommended as a standard treatment of symptomatic left-sided malignant colonic obstruction[44]. The guideline was updated in 2020, and SEMS used as a BTS is regarded as a treatment option in patients with potentially curable left-sided obstructing colon cancer as an alternative to emergency resection. SEMS is recommended as the preferred treatment for palliation of malignant colonic obstruction[4]. As the SEMS is gaining popularity, properly assessing OCRC patients who underwent stenting would be important. In this regard, the result of the present study suggested that obtaining GAR value might be as valuable as evaluating the TNM stage.

Obstruction is considered as one of the poor prognostic features for which adjuvant chemotherapy is recommended[11]. However, about half of the patients were not treated with adjuvant chemotherapy in this study, mainly due to advanced age and the patients' preference. The GAR status was significantly associated with the administration of adjuvant chemotherapy, but the GAR was not taken into consideration in the decision process. The Japanese guideline had not strongly recommended adjuvant chemotherapy for stage II CRC until 2019[45], which might have affected the decision. In fact, lymph node metastasis and administra-

tion of adjuvant chemotherapy were significantly correlated in the present cohort. The present result demonstrated that adjuvant chemotherapy was an independent prognostic factor for RFS after adjusting for variables including age, ASA score, and N stage. The patients who were administered the oxaliplatin-containing regimen did not develop recurrence in the study period. The addition of oxaliplatin is recommended for stage III and stage II patients with multiple high-risk factors in the NCCN guideline[11]. The results of the present study suggested that administering adjuvant chemotherapy, preferably with the oxaliplatin-containing regimen, might improve the long-term outcomes of OCRC patients.

The limitations in this study were the small sample size and the retrospective, non-randomized design in a single institution. The median follow-up time of 29 months was short to draw definitive conclusions regarding long-term outcomes. The patients were stage II and III OCRC cases who were inserted a SEMS and received curative surgery. They were a unique subset of CRC patients, and the results have to be interpreted with caution.

In summary, preoperative GAR was a significant prognostic indicator of RFS and CSS in OCRC patients who were inserted SEMS as a BTS. Multivariate analysis showed that GAR was an independent prognostic factor for RFS. The results suggested that evaluating both the TNM stage and GAR value might facilitate comprehensive assessment and tailored treatment of the OCRC patients.

#### Conflicts of Interest

There are no conflicts of interest.

#### Author Contributions

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

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

The protocol for this research project was approved by the ethics committee of the institution (#2019-0008), and it conforms to the provisions of the Declaration of Helsinki.

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