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Preoperative Pre-albumin Concentration as a Predictor of Short-term Outcomes in Elderly Patients With Colorectal Cancer

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Abstract. *Background/Aim: Population aging results in increasing numbers of elderly persons undergoing surgery for colorectal cancer. We sought to identify objective preoperative indicators of outcomes, with a view toward development of safe, effective treatments for such patients. Patients and Methods: The study included 99 patients aged 80 years or more, who were treated surgically for stage I–III colorectal cancer. Preoperative nutritional status was compared retrospectively between those who suffered postoperative complications (n=40) and those who did not (n=59). Results: Univariate analysis revealed low prealbumin (PreAlb) concentration (p=0.032) and low platelet-to-lymphocyte ratio (p=0.116) as risk factors for postoperative complications. Multivariate analysis showed preoperative PreAlb concentration to be an independent risk factor (OR=0.884; 95% confidence interval=0.791-0.989; p=0.024) associated with postoperative length of hospital stay (coef.=−0.336, p=0.002). Conclusion: PreAlb, a rapid turnover protein, shows promise as a simple predictor of postoperative complications in elderly patients treated for colorectal surgery.*

As the population ages, the number of elderly persons undergoing surgery for cancer is increasing, even among those aged 80 years or more. However, elderly patients with cancer are often compromised in terms of their general condition, physiological reserve, presence of one or more comorbidities, and/or nutritional status. Malnutrition can put patients at risk of infection, weaken their response to treatment, and lead to postoperative complications, and thus negatively influence their postoperative quality of life (1, 2). Patients' nutritional status is widely assessed clinically by measuring their serum total protein, albumin, lactate dehydrogenase, and total blood cholesterol concentrations (3). Studies have shown that nutritional status is a reliable predictor of outcomes after surgery for various types of cancer, with malnutrition associated with poor survival (4-7).

Counts of circulating white blood cells, including neutrophils, lymphocytes, and monocytes, have been shown to reflect patients' inflammatory status and an increase or decrease in the number of tissue macrophages and are thus useful for predicting clinical outcomes of patients undergoing surgery for colorectal cancer (8). Macrophages are considered to promote tumor progression in cases of colon cancer by producing tumor necrosis factor (TNF), which activates the Wnt–β-catenin pathway (9). Increased infiltration of macrophages into tumors is associated with both tumor angiogenesis and a poor postoperative outcome (10). The preoperative neutrophil-to-lymphocyte ratio (NLR) has been shown to predict clinical outcome in patients with stage II or III colon cancer (11), and the preoperative lymphocyte-to-monocyte ratio (LMR) has been shown to have prognostic value in cases of metastatic colon cancer (12). Like white blood cells, platelets are recruited to tumor sites and release proinflammatory mediators. Inflammation has been shown to play an important role in the pathogenesis and progression of colorectal cancer. Investigators have calculated the platelet-to-lymphocyte ratio (PLR) and neutrophil-platelet score (NPS) and showed

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these hematologic markers to be predictive of overall survival (13, 14).

Among immunonutrition system scores, the prognostic nutritional index (PNI) and the controlling nutritional status (CONUT) score, are attracting attention for use in patients with colorectal cancer. The PNI, first reported by Onodera *et al*. (15), is calculated on the basis of a patient's serum albumin concentration and peripheral lymphocyte count and is useful for predicting the prognosis of various cancers. Several studies have shown a low PNI to be an independent predictor of a poor prognosis for patients with colorectal cancer (16-18). The CONUT score, which is calculated on the basis of the serum albumin concentration, total cholesterol concentration, and peripheral lymphocyte count, has been shown to be associated with the host's nutritional and immune status (19). The CONUT score is widely used as a prognostic indicator in patients with various types of cancer, with the preoperative CONUT score being an independent risk factor for survival of and postoperative complications in patients with colorectal cancer (20, 21). Early turnover proteins such as prealbumin (PreAlb) and retinol binding protein (RBP), synthesized by the liver, have a fairly short half-life and quickly reflect a slight change in nutritional status, and can thus provide indirect information about the levels of visceral proteins as surrogate markers of nutritional status. PreAlb has a molecular weight of about 55,000 Daltons and a half-life of approximately 48 h (22). It is not only a marker of nutritional status; it is also an acute phase protein that serves as a marker of early-stage inflammation. Preoperative PreAlb has been shown to be an independent prognostic factor in many malignant diseases (22, 23). RBP is a glycoprotein with a molecular weight of about 22,000 and a half-life of 16 h. It binds to and transports retinol (vitamin A), and low levels appear to portend suboptimal outcomes in patients with postmenopausal breast cancer and patients with renal cell carcinoma (24, 25).

In terms of predicting postoperative outcomes in cases of colorectal cancer, the clinical usefulness of the many indicators mentioned above remains unclear, and we do not know which indicator would be especially useful in elderly patients, *i.e.,* patients aged 80 years or more. We conducted this retrospective observational study to identify and better understand factors associated with postoperative survival of patients aged 80 years or more and being treated for colorectal cancer, with a view toward development of safe and effective treatments for such patients.

Patients and Methods

Study patients. Patients aged 80 years or more who underwent elective surgery as preoperative diagnosis of Stage I to III colorectal cancer at Kanagawa Cancer Center between August 2016 and November 2020 were included. Patients with preoperative stage IV colon cancer, incomplete laboratory data, synchronous colon cancer, or emergency surgery were excluded. Of these, 99 patients were eligible for this analysis. All patients provided written, informed consent for their anonymized data to be used for study purposes, and the study was approved by the institutional review board of Kanagawa Cancer Center (Approval Number: 2020EKI-122).

Table I. *The controlling nutritional status (CONUT) score.*

Serum albumin (g/dl)	3.5-4.5	3.0-3.4	2.5-2.9	<2.5
Score	0	2	4	6
Total lymphocytes (/ml)	>1600	1,200-1,599	800-1,199	<800
Score	0	1	2	3
Total cholesterol (mg/dl)	>180	140-180	100-139	<100
Score	0	1	2	3
Total score	0-1	2-4	5-8	9-12
	Normal	Light	Moderate	Severe

The CONUT score is calculated on the basis of the serum albumin concentration, total blood cholesterol concentration, and total peripheral lymphocyte count. Normal: Normal nutrition; Light: light undernutrition; Moderate: moderate undernutrition; Severe: severe undernutrition.

Data collection. Patients' clinical characteristics [sex, age, body mass index (BMI), American Society of Anesthesiologists (ASA) score, and comorbidities including previous abdominal surgery], laboratory data, results of pathological investigation and perioperative data including short-term outcome were obtained from our hospital's electronic health records. Each patient's tumor had been classified preoperatively according to the tumor, node, and metastasis (TNM) staging system, and postoperative complications had been graded according to the Clavien-Dindo classification system (26). We obtained patients' preoperative laboratory data, including white blood cell count (WBC), neutrophil count, lymphocyte count, monocyte count, platelet count, hemoglobin concentration, total blood cholesterol, serum albumin, and C-reactive protein concentrations. Patients' NLR, LMR, PLR, PNI, CONUT score, and PreAlb and RBP concentrations were also obtained. The NLR was calculated by dividing the neutrophil count by the lymphocyte count. The LMR and PLR were calculated by dividing the lymphocyte count by the monocyte count and the platelet count by the lymphocyte count, respectively. The PNI was calculated from the albumin concentration and lymphocyte count as follows: PNI=10×ALB (g/dl)+0.005×lymphocyte count (per ml). The CONUT score was calculated on the basis of the albumin and total cholesterol concentrations, as shown in detail in Table I. Information obtained also included postoperative complications, taken as those occurring within 30 days after surgery and classified as Clavien-Dindo grade II or more, and postoperative length of hospital stay, taken as the number of complete or partial days spent in the hospital after surgery.

Statistical analysis. Continuous variables are shown as median (interquartile range [IQR]) values, and categorical variables are shown as the number (percentage) of patients, unless otherwise

indicated. Differences in continuous variables were analyzed by Wilcoxon/Kruskal-Wallis test, and differences in categorical variables analyzed by Fisher's exact test. Multiple logistic regression modeling was used to identify variables independently predictive of postoperative complications. Variables entered into the models were selected a priori on the basis of a review of the literature and our univariate analysis, when such analysis yielded a *p*-value<0.15. Odd ratios and 95% confidence intervals were calculated. Multiple linear regression analysis was also performed to examine relations between study variables and postoperative length of stay. The skewed distribution of hospital stay was normalized by means of logarithmic transformation to allow for entry of hospital stay into the regression model as a continuous variable; unstandardized and standardized coefficients (coef.) were produced. Multicollinearity was examined on the basis of the variance inflation factor (VIF), with a *p* value <5 considered significant. Receiver operating characteristic (ROC) curves were drawn to compare accuracy of the immunonutrition system scores as a predictor of postoperative complications, with results given as areas under the ROC curve (AUCs) and Youden's indices. All statistical analyses were performed with JMP 14 (SAS Institute Inc., Cary, NC, USA).

Results

The 99 study patients comprised 45 men and 44 women aged 82 years (range=81-85 years). Patients' basic clinical characteristics, comorbidities, preoperative blood test results, immunonutritional indicators, tumor characteristics, and operative variables, including short-term outcomes, are shown in Table II. One or more comorbidities were present in approximately 90% of patients, and immunonutritional status was low for a majority of patients, with the PreAlb concentration being 21.6 (17.5-23.8) mg/dl (normal=22.0-40.0 mg/dl) in 55 (50.5%) patients. The albumin concentration was low in this group (p=0.002), as was the hemoglobin concentration (p=0.018). Also low in this group were indicators of nutritional status, *i.e.,* the PNI (p=0.002), CONUT score (p=0.123), and the RBP concentration (p<0.001), as well as NLR (p=0.218) and PLR (p=0.054). The tumor was located in the right colon in 50.5% of patients. On pathological examination, the tumors were found to be of Stage II or more in 73% of cases. A total of 72 (72.7%) patients underwent laparoscopic surgery, however, conversion to open surgery was required in 2 cases (2.0%). Operation time was 247 (213-306) min. Postoperative hospital stay was 12 (9-16) days. Twenty-six patients in the low PreAlb group suffered a postoperative complication of Clavien-Dindo grade II or more, a rate that was much higher than that in the normal PreAlb group (52.7 % *vs*. 31.8%, respectively; p<0.119). Thus, postoperative hospital stay was significantly longer in the low PreAlb group than in the normal PreAlb group (13 days *vs*. 11 days; p=0.019).

Forty of the total patients suffered a Clavien-Dindo complication of grade II or more. Patients were divided into two groups: a "No complications" group (n=59) and a "Complications" group (n=40) (Table III). Common complications were postoperative bowel obstruction (n=11, 11.1%), urinary dysfunction (n=6, 6.1%), surgical site infection (n=5, 5.1%), postoperative delirium (n=5, 5.1%), and pneumonia (n=4, 4.0%). Anastomotic leakage occurred in approximately 3.0% of cases. There was no mortality. On univariate analysis, preoperative PreAlb (p=0.032), PLR (p=0.116), and tumor size (p=0.012) were found to be related to postoperative complications, but there was no difference in the prevalence of comorbidities, in oncological stage, or in the type of surgery between the two groups. Naturally, postoperative stay was significantly longer in the Complications group than in the No complications group (p<0.001). None of the other immunonutritional markers, including RBP, PNI, CONUT score, NLR, or LMR, was found to be associated with postoperative complications.

With albumin (5, 27, 28) and PNI (18, 29) having been identified previously as practical predictive indicators for postoperative complications, PreAlb, PNI, PLR, and tumor size were entered into our multiple logistic regression analysis, and PreAlb concentration and tumor size were found to be independent risk factors for postoperative complications (OR=0.884, 95%CI=0.791-0.989, p=0.024; OR=1.040, 95%CI=1.008-1.073, p=0.011) (Table IV). Postoperative length of stay was found to associate negatively with PreAlb concentration (coef.=–0.336, p=0.002) and positively with tumor size (coef.=0.208, p=0.063) (Table V) on multiple linear regression analysis. ROC curve analysis for accuracy of 7 immunonutritional markers in predicting postoperative complications showed PreAlb concentration to best predict such complications (AUC: 0.645; 95%CI=0.530-0.746, Youden index=0.289) (Table VI).

Discussion

Objective measures are now required in addition to careful consideration to establish whether surgical treatment is indicated for elderly persons, so that they do not miss the opportunity to receive appropriate treatment simply because of their age. Our aim in conducting this study was to evaluate short-term outcomes of surgery performed for colorectal cancer in patients aged 80 years or more and to determine the relation between nutritional status, immunological status, and surgical outcomes to identify factors predictive of a poor outcome.

We analyzed 7 factors, PreAlb, RBP, PNI, CONUT, NLR, PLR, and LMR, as potential predictors of postoperative complications in elderly patients with colorectal cancer. These indicators are reflective of undernutrition when it is present, and multivariate analysis showed low PreAlb concentration to be an independent predictor of a poor short-term outcome of elective surgery for colorectal cancer.

Table II. *Characteristics of patients and per preoperative PreAlb concentration.*

	Total patients (n=99)	Low PreAlb (n=55)	Normal PreAlb (n=44)	*p*-Value
Age, years	82 (81-85)	83 (81-86)	82 (81-83)	0.131
Male sex	45 (45.5)	15 (33.3)	30 (66.7)	<0.001
BMI, kg/m^2	21.6 (19.6-24.0)	21.6 (19.9-24.3)	21.4 (20.0-23.8)	0.964
ASA grade				0.742
0-2	91 (91.9)	51 (92.7)	40 (90.9)	
More than 3	8 (8.1)	4 (7.3)	4 (9.1)	
Comorbidities				
All	90 (90.9)	51 (92.7)	39 (88.6)	0.495
Hypertension	56 (56.6)	38 (69.1)	18 (40.9)	<0.001
Diabetes	15 (15.2)	10 (18.2)	5 (11.4)	0.347
Hyperlipidemia	15 (15.2)	6 (10.9)	9 (20.5)	0.188
Cardiovascular disease	9 (9.1)	3 (5.45)	6 (13.6)	0.159
Cerebrovascular disease	13 (13.1)	9 (16.4)	4 (9.1)	0.287
Previous abdominal surgery	42 (42.4)	19 (34.6)	23 (52.3)	0.076
Preoperative blood test results				
Albumin, g/dl	4.0 (3.7-4.2)	3.9 (3.6-4.1)	4.1 (3.9-4.3)	0.002
C-reactive protein, mg/dl	0.13 (0.07-0.26)	0.22 (0.09-0.40)	0.10 (0.05-0.14)	<0.001
Cholesterol, mg/dl	186 (165-208)	187 (167-209)	185.5 (163-207)	0.901
White blood cell, ×10^3/mm^3	5.50 (4.70-6.90)	5.60 (4.80-6.90)	5.45 (4.50-6.88)	0.568
Neutrophil, ×10^3/mm^3	3.46 (2.77-4.69)	3.50 (2.95-4.94)	3.43 (2.69-4.39)	0.554
Lymphocyte, ×10^3/mm^3	1.38 (1.13-1.75)	1.35 (1.13-1.63)	1.47 (1.13-2.08)	0.329
Monocyte, ×10^3/mm^3	0.31 (0.23-0.38)	0.31 (0.22-0.39)	0.32 (0.24-0.37)	0.880
Hemoglobin, ×10^3/mm^3	12.1 (10.8-13.1)	11.7 (10.0-12.7)	12.5 (11.4-13.5)	0.018
Platelet, ×104/mm^3	23.0 (19.3-27.1)	23.9 (19.8-28.4)	22.2 (18.6-26.1)	0.222
Immunonutritional indicators				
PNI	47.6 (43.9-49.7)	46.8 (41.2-49.1)	49.0 (45.9-50.8)	0.002
CONUT score	1.0 (1.0-2.0)	1.0 (1.0-3.0)	1.0 (1.0-2.0)	0.123
Retinol binding protein, mg/dl	2.9 (2.4-3.2)	2.5 (2.1-3.0)	3.2 (2.9-3.8)	<0.001
NLR	2.32 (1.86-3.40)	2.68 (1.90-3.50)	2.29 (1.78-3.17)	0.218
PLR	155 (120-208)	176 (126-228)	134 (109-193)	0.054
LMR	5.00 (3.65-6.51)	4.87 (3.41-6.59)	5.04 (4.17-6.50)	0.593
Oncological characteristics				
Tumor location				0.472
Right colon	50 (50.5)	26 (47.3)	24 (54.6)	
Left colon	49 (49.5)	29 (52.7)	20 (45.4)	
Treated pathological stage				0.089
0	5 (5.1)	1 (1.8)	4 (9.1)	
I	22 (22.2)	9 (16.4)	13 (29.6)	
II	26 (26.3)	18 (32.7)	8 (18.2)	
III	44 (44.4)	25 (45.5)	19 (43.2)	
IV	2 (2.0)	2 (3.6)	0 (0.0)	
Tumor size, mm	40.0 (30.0-55.0)	35.0 (20.0-45.0)	45.0 (35.0-60.0)	<0.001
No. of dissected lymph nodes	28.0 (19.0-40.0)	28.0 (21.0-39.0)	28.5 (17.5-42.5)	0.813
Operative details				
Type of surgery				0.659
Open	27 (27.3)	16 (29.1)	11 (25.0)	
Laparoscopy	72 (72.7)	39 (70.9)	33 (75.0)	
Operation time, min	247 (213-306)	247 (210-305)	246 (218-308)	0.838
Blood loss volume, ml	45.0 (15.0-115.0)	40.0 (10.0-90.0)	47.5 (20.0-150.0)	0.285
Major complications				0.119
Yes (more than grade II)	40 (40.4)	26 (52.7)	14 (31.8)	
No (less than grade I)	59 (59.6)	29 (47.3)	30 (68.2)	
Postoperative stay, days	12 (9-16)	13 (10-18)	11 (9-14)	0.019
Postoperative mortality	0 (0.0)	0 (0.0)	0 (0.0)	NA

BMI: Body mass index; ASA: American Society of Anesthesiologists; PNI: prognostic nutritional index; CONUT: Controlling Nutritional Status; NLR: neutrophil-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio; LMR: lymphocyte-to-monocyte ratio; NA: not applicable. Median (interquartile range) value or number (percentage) of patients is shown, unless otherwise indicated.

Table III. *Results of univariate analysis of risk factors for postoperative complications in the "No complications" and "Complications" groups.*

	No complications (n=59)	Complications (n=40)	*p*-Value
Age, years	83 (81-84)	82 (81-85)	0.809
Male sex	24 (40.7)	21 (52.5)	0.246
BMI, kg/m^2	21.6 (19.6-24.9)	21.2 (19.3-23.4)	0.356
ASA grade			0.184
0-2	56 (94.9)	35 (87.5)	
≥3	3 (5.1)	5 (12.5)	
Comorbidities			
All	53 (89.8)	37 (92.5)	0.650
Hypertension	35 (59.3)	21 (52.5)	0.502
Diabetes	8 (13.6)	7 (17.5)	0.592
Hyperlipidemia	12 (20.3)	3 (7.5)	0.080
Cardiovascular disease	9 (15.3)	0 (0)	<0.001
Cerebrovascular disease	6 (10.2)	7 (17.5)	0.289
Previous abdominal surgery	24 (40.1)	18 (45.0)	0.669
Preoperative blood test results			
Albumin, g/dl	4.0 (3.7-4.2)	3.9 (3.6-4.2)	0.498
C-reactive protein, mg/dl	0.13 (0.08-0.26)	0.15 (0.06-0.26)	0.870
Cholesterol, mg/dl	192 (167-211)	182.5 (161-206)	0.143
White blood cells, ×10^3/mm^3	5.30 (4.70-6.60)	6.20 (4.63-7.05)	0.267
Neutrophils, ×10^3/mm^3	3.40 (2.78-4.35)	3.74 (2.78-5.03)	0.468
Lymphocytes, ×10^3/mm^3	1.37 (1.05-1.73)	1.40 (1.18-1.86)	0.635
Monocytes, ×10^3/mm^3	0.28 (0.23-0.35)	0.32 (0.23-0.47)	0.357
Hemoglobin, g/dl	12.0 (11.0-13.1)	12.3 (10.1-13.0)	0.965
Platelets, ×10^4/mm^3	22.4 (20.0-27.1)	23.5 (18.3-27.7)	0.817
Immunonutritional indicators			
Prealbumin, mg/dl	21.9 (18.9-25.3)	19.8 (16.7-23.4)	0.032
Retinol binding protein, mg/dl	2.9 (2.4-3.6)	2.7 (2.3-3.1)	0.251
PNI	47.8 (44.1-49.8)	46.9 (42.9-49.7)	0.357
CONUT score	1.0 (1.0-2.0)	1.0 (1.0-2.0)	0.710
NLR	2.33 (1.84-3.29)	2.30 (1.87-3.56)	0.822
PLR	154 (119-202)	161 (118-215)	0.116
LMR	5.00 (4.00-6.50)	4.70 (3.61-6.53)	0.542
Oncological characteristics			
Tumor location			0.622
Right colon	28 (47.5)	21 (52.5)	
Left colon	31 (52.5)	19 (47.5)	
Treated pathological stage			0.503
0	4 (6.8)	1 (2.5)	
I	16 (27.1)	6 (15.0)	
II	14 (23.7)	12 (30.0)	
III	24 (40.7)	20 (50.0)	
IV	1 (1.7)	1 (2.5)	
Tumor size, mm	35 (20-45)	45 (35-59)	0.012
No. of dissected lymph nodes	28 (21-40)	29 (15-43)	0.850
Operative details			
Type of surgery			0.617
Open	15 (25.4)	12 (30.0)	
Laparoscopy	44 (74.6)	28 (70.0)	
Operation time, min	243 (214-281)	274 (204-328)	0.160
Blood loss volume, ml	40 (10-90)	50 (20-195)	0.221
Postoperative stay, days	10 (9-12)	17 (14-22.5)	<0.001
Postoperative mortality	0 (0.0)	0 (0.0)	NA

BMI: Body mass index; ASA: American Society of Anesthesiologists; PNI: prognostic nutritional index; CONUT: Controlling Nutritional Status; NLR: neutrophil-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio; LMR: lymphocyte-to-monocyte ratio; NA: not applicable. Median (interquartile range) value or number (percentage) of patients is shown, unless otherwise indicated.

Table IV. *Results of multivariable logistic regression analysis of risk factors for postoperative complications.*

	p-Value	OR	95%CI
Albumin	0.177	4.845	(0.443-53.04)
Prealbumin	0.024	0.884	(0.791-0.989)
PNI	0.375	0.922	(0.763-1.113)
PLR	0.046	0.993	(0.986-1.001)
Tumor size	0.011	1.040	(1.008-1.073)

OR: Odds ratio; CI: confidence interval; PNI: prognostic nutritional index; PLR: platelet-to-lymphocyte ratio.

Table V. *Results of multiple linear regression analysis of factors associated with log-transformed postoperative length of stay.*

	Unstandardized coefficient	Standard error	Standardized coefficient	*p*-Value	VIF
(constant)	2.611	0.536			
Albumin	0.034	0.180	0.031	0.849	3.149
Prealbumin	–0.027	0.009	–0.336	0.002	1.328
PNI	0.006	0.013	0.083	0.643	3.744
PLR	–0.000	0.001	–0.110	0.367	1.698
Tumor size	0.005	0.002	0.208	0.063	1.411

PNI: Prognostic nutritional index; PLR: platelet-to-lymphocyte ratio; VIF: variance inflation factor.

Table VI. *Predictive accuracy of immunonutritional systemic scores for postoperative complications as shown by receiver operating characteristic (ROC) curve analysis.*

	AUC	95%CI	Youden index
Prealbumin	0.645	0.530-0.746	0.289
Retinol binding protein	0.570	0.454-0.678	0.220
PNI	0.545	0.426-0.659	0.180
CONUT score	0.521	0.412-0.628	0.069
NLR	0.525	0.410-0.639	0.142
PLR	0.524	0.409-0.635	0.126
LMR	0.543	0.424-0.657	0.180

AUC: Area under the ROC curve; 95%CI: 95% confidence interval; PNI: prognostic nutritional index; CONUT: controlling nutritional status; NLR: neutrophil-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio; LMR: lymphocyte-to-monocyte ratio.

Patient's PreAlb concentration is one of several indicators of a patient's nutritional status. Another name for PreAlb is transthyretin. The name transthyretin is derived from the protein's activity as a carrier of the thyroid hormone hyroxine (30), but because it appears on the anode side of albumin under electrophoresis, it is also called prealbumin. PreAlb is affected by the same factors that affect albumin, but the advantage of using PreAlb is that its half-life is shorter than that of albumin, so it sensitively reflects a patient's nutritional status and rapidly responds to a change in nutritional status. It takes about 3 weeks for the albumin levels to rise after nutritional intervention, but PreAlb increases within a few days. Malnutrition is associated with an increased risk of complications and with mortality (31); therefore, it is very useful to accurately determine a patient's nutritional status, and PreAlb is often used to evaluate patients' nutritional status and predict outcomes of those with a malignant tumor. In the gastrointestinal field, it has been reported that preoperative serum PreAlb concentration is a useful and independent marker for predicting the occurrence of postoperative complications of patients with gastric cancer (22, 32), esophageal cancer (33), and colorectal cancer (34). Although there are various reports of association between PreAlb concentration and surgical outcomes, few pertain specifically to outcomes of surgery performed for colorectal cancer, especially in elderly patients. To our knowledge, ours is the first study to show correlation between preoperative PreAlb concentration and short-term outcomes of surgery performed for colorectal cancer in patients aged 80 years or more.

Because elderly patients tend to have poor physiological reserve, PreAlb concentration, which can reflect recent nutritional status and be used to detect nutritional deficits with its short half-life of 48 h, may be suitable for nutritional assessment in elderly patients. In fact, for the multivariable logistic regression analysis, we selected, on the basis of previous reports, albumin, with its 21-day serum half-life, and PNI, which combines information on albumin and lymphocytes, as priori variables for association with postoperative complications. However, neither was found to be strongly associated with postoperative outcomes of elderly patients. In addition to the multivariable regression analysis for complications and length of hospital stay, ROC curve analysis showed that PreAlb concentration could accurately predict the occurrence of one or more postoperative complications and functioned better than the other markers tested (Table VI). The results of our study indicate that PreAlb is more reliable and sensitive marker for prediction of outcomes than other variables examined for elderly patients requiring surgery for colorectal cancer.

Our study is limited by the fact that we sought to identify risk factors for postoperative complications among preoperative patient characteristics. Neither the surgical procedure nor the pathological tumor stage, either of which indeed might influence outcomes, was included as candidate variables.

Although it has been indicated that the incidence of surgery-related complications increases when preoperative nutritional status is poor (1, 2), there is no consensus on perioperative nutrition therapy for malnourished patients. PreAlb has a short serum half-life and is thought to

sensitively detect changes in nutritional status. If feasible, optimizing the nutritional status of patients with a low PreAlb concentration may be considered before rather than after surgery. Currently, there is no evidence that nutrition therapy can reduce the risk of postoperative complications or improve patient survival. We think, however, that if we can intervene with nutritional support before surgery, a low preoperative PreAlb concentration may be a risk factor that can be modified to lower patients' risk of postoperative complications. Some risk factors, such as sex and the presence of comorbidities are difficult if not impossible to change, we hope that future studies will indicate that preoperative nutritional intervention for patients with a low preoperative PreAlb concentration can reduce the incidence of postoperative complications.

As the number of elderly patients with colorectal cancer increases, it will become more and more difficult to judge which cases are indicated for surgical treatment. Physical strength and the presence of comorbidities vary greatly between individual patients, thus it is not possible to determine indications for surgery based solely on the patient's age. Our study data indicate that preoperative PreAlb concentration is useful for predicting postoperative complications in patients with colorectal cancer who are aged 80 years or more. There are few facilities where PreAlb is measured routinely, and therefore the usefulness of PreAlb has not garnered much attention. We hope that it will be measured preoperatively at many facilities in the future. A low PreAlb concentration suggests increased surgical risk, and PreAlb can be measured simply along with other blood tests. Because the postoperative course is always a matter of concern, especially for elderly patients, both patients and surgeons would be helped to prepare for postoperative complications if the preoperative PreAlb concentration is determined before surgery.

Conflicts of Interest

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

Authors' Contributions

Study conception and design: S Sato, M Shiozawa, T Oshima; Acquisition of data: S Sato, S Nukada, K Iguchi, K Kazama; Analysis and interpretation of data: S Sato, Y Atsumi, M Numata, H Tamagawa; Manuscript writing: All Authors; Critical revision and final approval of manuscript: S Sato, K Tanaka, Y Rino.

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