



Elevated prealbumin levels after preoperative nutritional intervention is an independent prognostic factor for overall survival after radical gastrectomy in patients with gastric cancer and severe malnutrition

Ryota Matsui¹ · Souya Nunobe¹ · Motonari Ri¹ · Rie Makuuchi¹ · Tomoyuki Irino¹ · Masaru Hayami¹ · Manabu Ohashi¹ · Takeshi Sano¹

Received: 13 January 2025 / Accepted: 16 June 2025
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Abstract

Purpose This study aimed to clarify the effects of preoperative nutritional intervention on long-term survival after radical gastrectomy in patients with severe malnutrition.

Methods This retrospective cohort study included consecutive patients who underwent radical gastrectomy for primary stages I–III gastric cancer between August 2010 and December 2021. The primary outcome measure was overall survival (OS). We compared OS between the groups with and without nutritional intervention. In the intervention group, we compared OS between the groups with and without nutritional improvement. Prognostic factors were identified using the Cox proportional hazards regression analysis.

Results Median follow-up duration was 51 months. Of the 118 patients, 35 (29.7%) and 83 (70.3%) were in the group without and with nutritional intervention, respectively. Of the 83 patients in the group with nutritional intervention, 24 (28.9%) were classified as group without elevated prealbumin levels and 59 (71.1%) as group with elevated prealbumin levels. There was no difference in OS between the groups with and without nutritional intervention ($P=0.532$); however, there was a trend toward better OS in the group with elevated prealbumin levels than in the group without elevated prealbumin levels ($P=0.181$). Multivariate analysis showed that elevated prealbumin levels after intervention was an independent, favorable, prognostic factor for OS (hazard ratio, 0.320; 95% confidence interval, 0.112–0.917; $P=0.030$).

Conclusions Preoperative nutritional therapy in patients with severe malnutrition does not contribute to long-term survival after gastrectomy. However, in patients who have undergone nutritional therapy, prognosis could be predicted by elevated prealbumin levels.

Keywords Gastric cancer · Nutritional intervention · Overall survival · Prealbumin · Prognosis

Introduction

Severe malnutrition leads to poor postoperative outcomes in cancer patients [1–3]. The Global Leadership Initiative on Malnutrition (GLIM) criteria, new diagnostic criteria for malnutrition, were published in 2019 [4], and a meta-analysis has shown that severe malnutrition, as defined by

the GLIM criteria, increases postoperative complications and results in poor overall survival [3, 5–7]. To improve postoperative outcomes, the European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines recommend preoperative nutritional intervention for 7–14 days for severely undernourished patients [8, 9]. Therefore, physicians and dietitians should not only diagnose malnutrition preoperatively using the diagnostic criteria for malnutrition but also appropriate preoperative nutritional interventions.

The impact of preoperative nutritional intervention on long-term survival after radical gastrectomy in patients with GLIM-defined severe malnutrition remains unclear. One problem is the absence of good indicators to determine whether the nutritional status has improved after nutritional

✉ Souya Nunobe
souya.nunobe@jfcf.or.jp

¹ Department of Gastroenterological Surgery, The Cancer Institute Hospital of Japanese Foundation for Cancer Research, 3-8-31, Ariake, Koto-ku, Tokyo 135- 8550, Japan

intervention for 7–14 days, as recommended by the guidelines. As an indicator of nutritional improvement, prealbumin has attracted attention as a dynamic nutritional indicator due to its short half-life [10–12]. We previously reported that improvement in prealbumin levels by preoperative nutritional intervention reduced postoperative complications [13]. However, it remains unclear whether improving prealbumin levels in severely undernourished patients prolongs long-term survival.

This study aimed to investigate the impact of preoperative nutritional intervention on long-term survival after radical gastrectomy in patients with GLIM-defined severe malnutrition. Notably, the optimal value of prealbumin as an indicator of nutritional improvement is yet to be determined. Therefore, if the cutoff value of prealbumin that leads to an improved prognosis is identified in this study, it is expected to lead to a new index for monitoring nutritional interventions.

Methods

Study design

This retrospective cohort study was conducted at the Cancer Institute Hospital of the Japanese Foundation for Cancer Research to evaluate patients with primary gastric cancer who underwent radical gastrectomies between August 2010 and December 2021. The study included patients diagnosed with GLIM-defined severe malnutrition and stage I–III gastric cancer, according to the 15th edition of the Japanese Classification of Gastric Carcinoma [14]. The study excluded patients (i) without GLIM-defined severe malnutrition, (ii) with remnant gastric cancer, (iii) with multiple cancers, (iv) who had undergone noncurative resection, and (v) who were undergoing neoadjuvant chemotherapy. Clinical data, blood samples, and pathological findings were retrospectively collected from the hospital's electronic medical records.

All experimental protocols described in this study were approved by the Institutional Ethical Review Committee (authorization number:2022-GB-078), met the ethical guidelines of the Japan Ministry of Health, Labor, and Welfare for Medical and Health Research Involving Human Subjects, and conformed to the provisions of the Declaration of Helsinki. Patient consent was obtained using an opt-out recruitment method for all patients who declined participation.

Definition of malnutrition

In this study, malnutrition and its severity were diagnosed using body mass index (BMI) and body weight loss (BWL) rate according to GLIM criteria [4] as follows: severe malnutrition as a BWL rate > 10% within the past 6 months or > 20% beyond 6 months, or a BMI of < 18.5 kg/m² if < 70 years old or < 20.0 kg/m² if > 70 years old. We excluded patients with or without malnutrition.

Outcomes

The primary outcome was the overall survival (OS), which was defined as the time between surgery and death. The secondary outcome was recurrence-free survival (RFS), defined as the time between surgery and either recurrence or death, whichever occurred first. For patients who were not followed up at the authors' hospital, the hospital staff surveyed the public office 5 years postoperatively to determine whether the patient was alive or had died of gastric cancer or other diseases. Postoperative complications were defined as complications of Clavien-Dindo classification [15] grade ≥ 2 occurring within 30 days postoperatively.

First, long-term survival was compared between groups with and without nutritional intervention. Next, in the nutritional intervention group, we compared long-term survival between the groups with and without nutritional improvement. In this study, prealbumin level was used as an indicator of nutritional improvement.

Perioperative nutritional management

Preoperative nutritional intervention consisted mainly of enteral nutrition at 30 kcal/kg/day for 7–14 days. When enteral nutrition alone was insufficient to meet the patient's caloric needs, parenteral nutrition was used to supplement the diet. The composition of the enteral nutritional supplements was standard without immunonutrients.

All the patients followed the same clinical pathway for perioperative management. The nasogastric tube was removed before the patient was discharged from the operating room. Oral intake was initiated on postoperative day (POD) 1, beginning with water. The patients began to eat solid food on POD 3, starting with rice gruel and soft food on POD 4, and advancing in three steps to regular food intake on POD 5.

For nutritional intervention after discharge, we provided oral nutritional supplements to patients who did not increase their food intake. However, we did not provide a uniform intervention for all patients. Postoperative nutritional support was promptly discontinued when the patient's food intake sufficiently increased.

Treatment strategy

During the study period, open gastrectomy with D2 lymph node dissection was indicated in patients with cT2 or deeper gastric cancer, whereas laparoscopic gastrectomy with D1+lymph node dissection was indicated in patients with cT1 gastric cancer. Following gastrectomy, various types of reconstruction were performed. Typically, Billroth I or Roux-en-Y is selected for distal gastrectomy, Roux-en-Y for total gastrectomy, gastrogastrostomy for pylorus-preserving gastrectomy, and jejunal interposition or esophagogastrotomy for proximal gastrectomy.

In pStages II-III, postoperative adjuvant chemotherapy was started with S-1 or DS (docetaxel plus S-1), with dose reductions according to the guidelines if side effects were observed; S-1 and DS were continued for up to 1 year. Postoperative adjuvant chemotherapy was discontinued when side effects could not be controlled by dose optimization, two or more dose reductions, or confirmed recurrence of gastric cancer during adjuvant chemotherapy. No other treatment was administered until recurrence. Patients who relapsed were treated according to the Japanese gastric cancer treatment guidelines [16, 17]. In this study, completion of adjuvant chemotherapy was defined as continuation of adjuvant chemotherapy for one year.

Statistical analysis

The Mann-Whitney U test was used to analyze continuous variables. Chi-squared or Fisher's exact tests were used to analyze categorical variables, and the log-rank test was used in the Kaplan-Meier survival analysis for OS and RFS. Multivariate analysis with Cox proportional hazards regression was used to identify the prognostic factors and calculate hazard ratios (HRs). All statistical analyses were performed using EZR software (Saitama Medical Center, Jichi Medical University, Saitama, Japan). Statistical significance was set at $P < 0.05$.

Results

Patient characteristics

The median follow-up period was 51 months (interquartile range, 21–73). A flowchart of the study is shown in Fig. 1. Of the 118 patients who were eligible, 35 (29.7%) were in the group without nutritional intervention and 83 (70.3%) in the group with nutritional intervention. Of the 83 patients in the group with nutritional intervention, 24 (28.9%) were classified into the non-elevated prealbumin levels group and 59 (71.1%) into elevated prealbumin levels group.

A comparison of the patient backgrounds is shown in Table 1. In a comparison of groups with and without nutritional intervention, the group with nutritional intervention had significantly higher BMI ($P = 0.021$), more advanced cStage and pStage ($P < 0.001$, $P < 0.001$, respectively), and higher prealbumin levels just before surgery ($P < 0.001$). In

Fig. 1 The design of this study

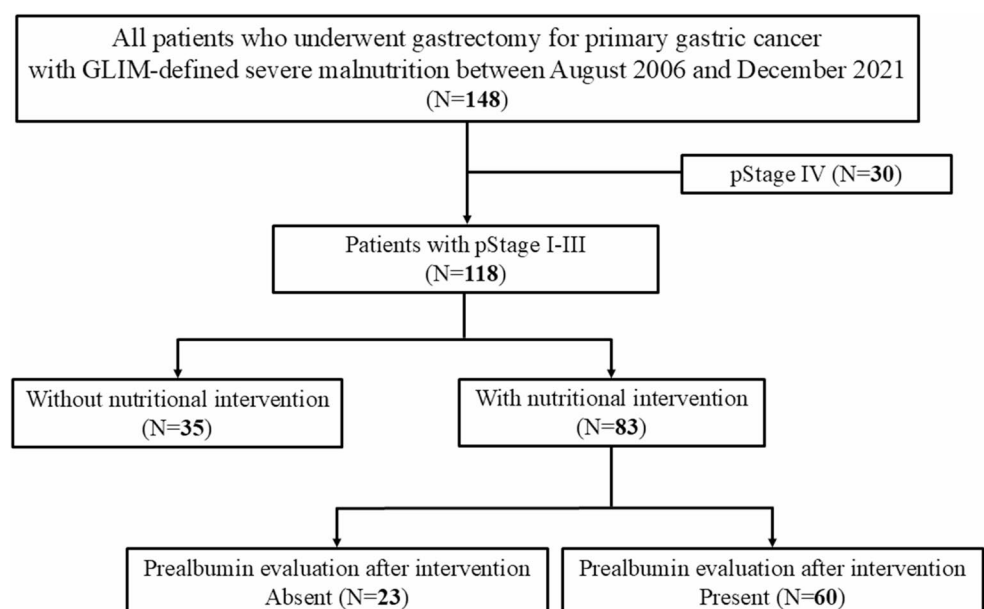


Table 1 Patient characteristics

	Nutritional intervention			Elevated prealbumin levels after intervention		
	Without intervention (N=35)	With intervention (N=83)	P value	Absent (N=24)	Present (N=59)	P value
Sex						
Male	19 (54.3%)	44 (53.0%)	1.000	11 (45.8%)	33 (55.9%)	0.471
Female	16 (45.7%)	39 (47.0%)		13 (54.2%)	26 (44.1%)	
Age (years), Median (IQR)	77.0 (68.0, 80.0)	72.0 (66.0, 80.0)	0.102	75.0 (64.0, 79.0)	71.0 (66.0, 80.0)	0.823
BMI (kg/m ²), Median (IQR)	18.1 (17.5, 19.2)	19.5 (17.8, 21.4)	0.021	20.6 (17.7, 22.8)	19.0 (17.8, 21.2)	0.248
Nutritional intervention period (Days), Median (IQR)		10.0 (7.0, 13.3)		9.0 (6.0, 13.0)	10.0 (8.0, 14.0)	0.215
Nutritional dose (kcal/day) Median (IQR)		1600 (1410, 1800)		1600 (1420, 1845)	1600 (1410, 1800)	0.979
Comorbidity						
Chronic kidney disease	7 (20.0%)	7 (8.4%)	0.116	2 (8.3%)	5 (8.5%)	1.000
Diabetes	4 (11.4%)	12 (14.5%)	0.775	7 (29.2%)	5 (8.5%)	0.033
Clinical stage						
I	13 (37.1%)	2 (2.4%)		1 (4.2%)	1 (1.7%)	
II	5 (14.3%)	32 (38.6%)	<0.001	6 (25.0%)	26 (44.1%)	
III	15 (42.9%)	44 (53.0%)		14 (58.3%)	30 (50.8%)	0.147
IVA	2 (5.7%)	5 (6.0%)		3 (12.5%)	2 (3.4%)	
Surgical approach						
Laparoscopic surgery	7 (20.0%)	4 (4.8%)		2 (8.3%)	2 (3.4%)	
Open surgery	28 (80.0%)	79 (95.2%)	0.015	22 (91.7%)	57 (96.6%)	0.575
Surgical procedure						
Distal gastrectomy	22 (62.9%)	65 (78.3%)		15 (62.5%)	50 (84.7%)	
Total gastrectomy	13 (37.1%)	18 (21.7%)	0.046	9 (37.5%)	9 (15.3%)	0.039
Lymph node dissection						
D1+	12 (34.3%)	8 (9.6%)		3 (12.5%)	5 (8.5%)	
D2	23 (65.7%)	75 (90.4%)	0.002	21 (87.5%)	54 (91.5%)	0.685
CRP (mg/dL), Median (IQR) ≥ 0.5 mg/dL	0.75 (0.29, 2.38)	0.35 (0.15, 1.07)	0.059	0.40 (0.18, 3.90)	0.33 (0.14, 0.97)	0.319
	8 (22.9%)	28 (33.7%)	<0.001	6 (25.0%)	22 (37.3%)	<0.001
Prealbumin before intervention (mg/dL), Median (IQR)		15.4 (11.0, 18.7)		15.4 (12.0, 24.1)	15.3 (10.8, 17.4)	0.223
Prealbumin just before surgery (mg/dL), Median (IQR)	12.7 (10.4, 14.2)	16.4 (12.8, 22.9)	<0.001	13.1 (9.2, 15.8)	19.2 (14.7, 23.0)	0.001
Serosal invasion	17 (48.6%)	64 (77.1%)	0.004	17 (73.9%)	47 (78.3%)	0.772
Lymph node metastasis						
N1	6 (17.1%)	13 (15.7%)	0.026	3 (13.0%)	10 (16.7%)	0.845
N2	8 (22.9%)	23 (27.7%)		5 (21.7%)	18 (30.0%)	
N3	4 (11.4%)	27 (32.5%)		9 (39.1%)	18 (30.0%)	
Pathological stage						
I	15 (42.9%)	5 (6.0%)	<0.001	1 (4.2%)	4 (6.8%)	0.917
II	5 (14.3%)	18 (21.7%)		6 (25.0%)	11 (18.6%)	
III	15 (42.9%)	60 (72.3%)		17 (70.8%)	44 (74.6%)	
Histological type						
Differentiated	17 (48.6%)	28 (33.7%)	0.150	9 (37.5%)	19 (32.2%)	0.798
Undifferentiated	18 (51.4%)	55 (66.3%)		15 (62.5%)	40 (67.8%)	
Postoperative complications						
Overall complications	5 (14.3%)	28 (33.7%)	0.043	8 (33.3%)	20 (33.9%)	1.000
Severe complications	2 (5.7%)	12 (14.5%)	0.226	5 (20.8%)	7 (11.9%)	0.315
Adjuvant chemotherapy	8 (22.9%)	46 (55.4%)	0.001	14 (58.3%)	32 (54.2%)	0.810
Dose reduction	4 (11.4%)	22 (26.5%)	0.006	9 (37.5%)	13 (22.0%)	0.337
Completion	4 (11.4%)	30 (36.1%)	0.004	7 (29.2%)	23 (39.0%)	0.337

BMI body mass index, CRP C-reactive protein, IQR interquartile range

a comparison of prealbumin elevations after intervention, group with elevated prealbumin levels had more patients with $\text{CRP} \geq 0.5$ mg/dL ($P < 0.001$), and higher prealbumin levels just before surgery ($P < 0.001$), but no difference in duration and dose of nutritional intervention ($P = 0.215$, $P = 979$, respectively).

OS and RFS

A comparison of the OS between the groups with and without nutritional intervention is shown in Fig. 2. No significant differences were found between the groups with and without nutritional intervention ($P = 0.532$, Fig. 2a). When stratified by pStage, there were no statistically significant

differences for OS in pStage I or II ($P = 0.770$, Fig. 2b), and pStage III ($P = 0.532$, Fig. 2c).

A comparison of RFS between the groups with and without nutritional intervention is shown in Fig. 3. No significant differences were found between the groups with and without nutritional intervention ($P = 0.454$, Fig. 3a). When stratified by pStage, there were no statistically significant differences for RFS in pStage I or II ($P = 0.598$, Fig. 3b), and pStage III ($P = 0.454$, Fig. 3d).

A comparison of long-term survival in patients with severe malnutrition who underwent nutritional intervention is shown in Fig. 4. There was a trend toward better OS ($P = 0.181$, Fig. 4a) and RFS ($P = 0.241$, Fig. 4b) in the group with elevated prealbumin levels after nutritional intervention than in the group without elevated prealbumin levels.

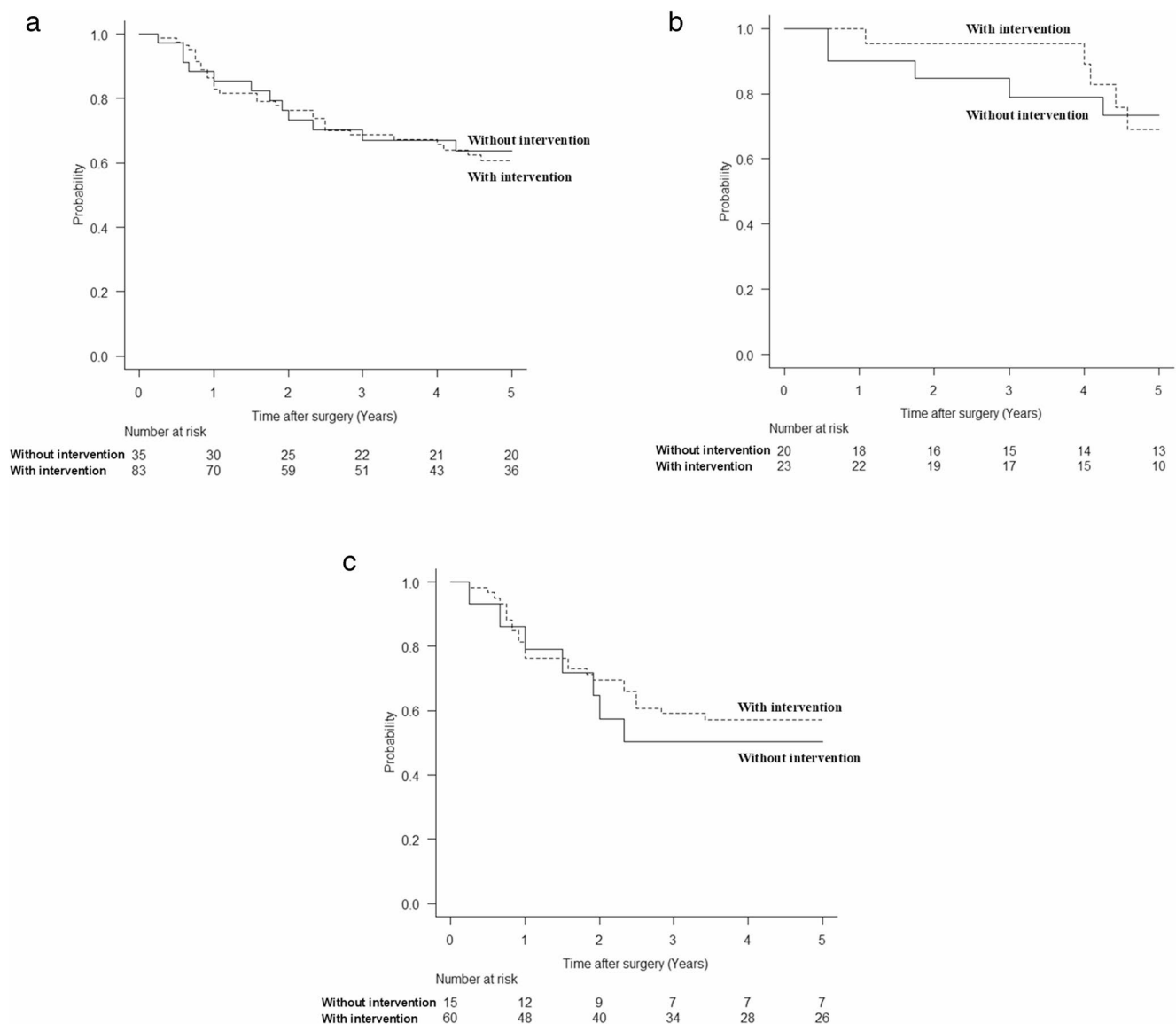


Fig. 2 Comparison of overall survival in patients with severe malnutrition between groups with and without nutritional intervention. **a)** In all patients **b)** In pStage I or II **c)** In pStage III

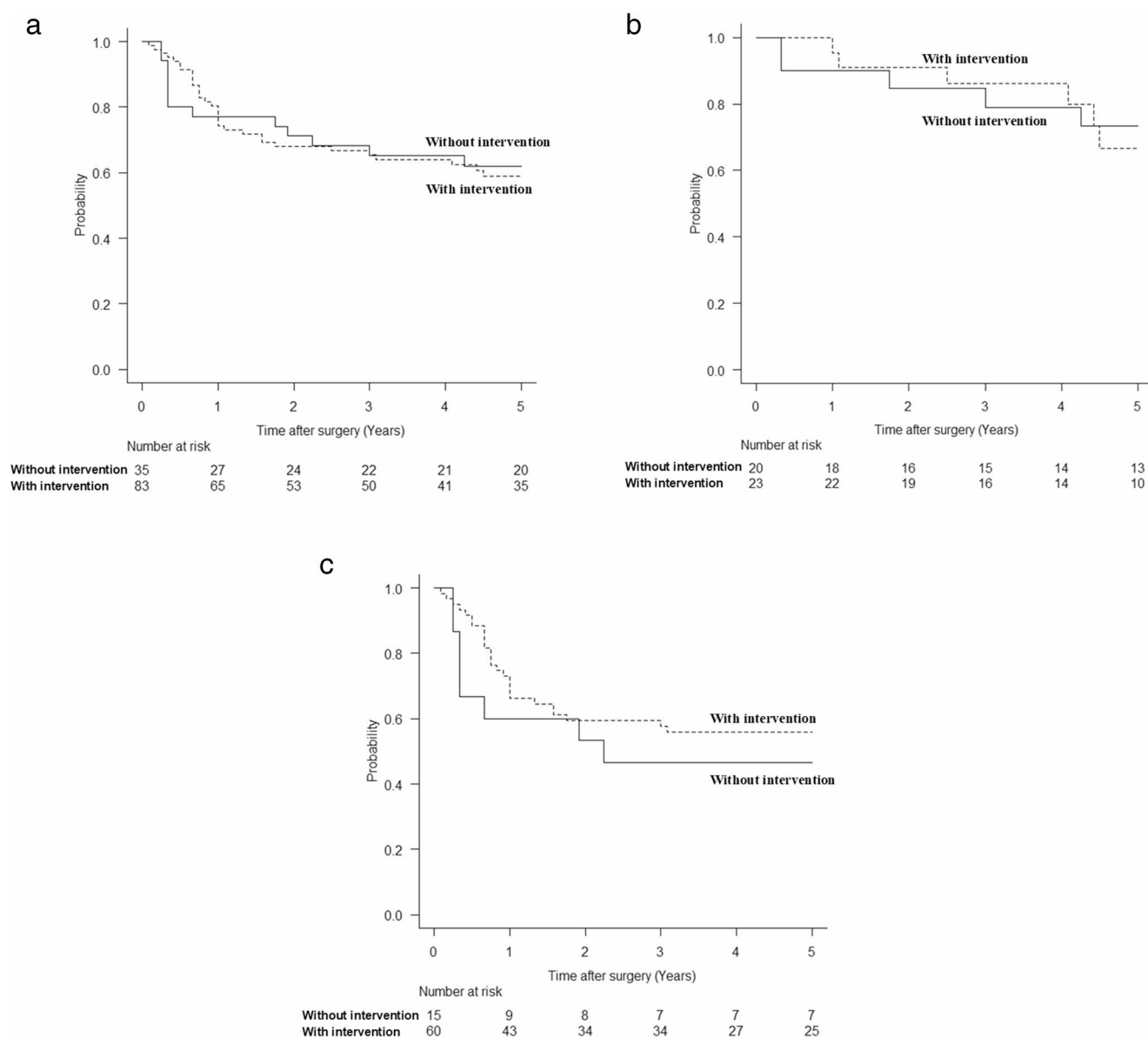


Fig. 3 Comparison of recurrence-free survival in patients with severe malnutrition between groups with and without nutritional intervention. **a)** In all patients **b)** In pStage I or II **c)** In pStage III

Prognostic factors according to multivariate analysis results

Table 2 shows the results of the multivariate analysis of OS in all patients. The elevated prealbumin levels after nutritional intervention was found to be an independent favorable prognostic factor for OS (HR: 0.320, 95% confidence interval (CI): 0.112–0.917, $P=0.034$).

Table 3 shows the results of the multivariate analysis of RFS in all patients. The elevated prealbumin levels after nutritional intervention was found to be an independent favorable prognostic factor for RFS (HR: 0.259, 95% CI: 0.094–0.715, $P=0.009$).

Discussion

This study examined the impact of preoperative nutritional intervention on the long-term survival of patients with gastric cancer undergoing radical gastrectomy for severe malnutrition, as defined by the GLIM criteria. Long-term survival did not differ between the groups with and without nutritional intervention, but among the groups with nutritional intervention, there was a trend toward better long-term survival in the group with elevated prealbumin levels than in the group without elevated prealbumin levels. Elevated prealbumin levels after nutritional intervention

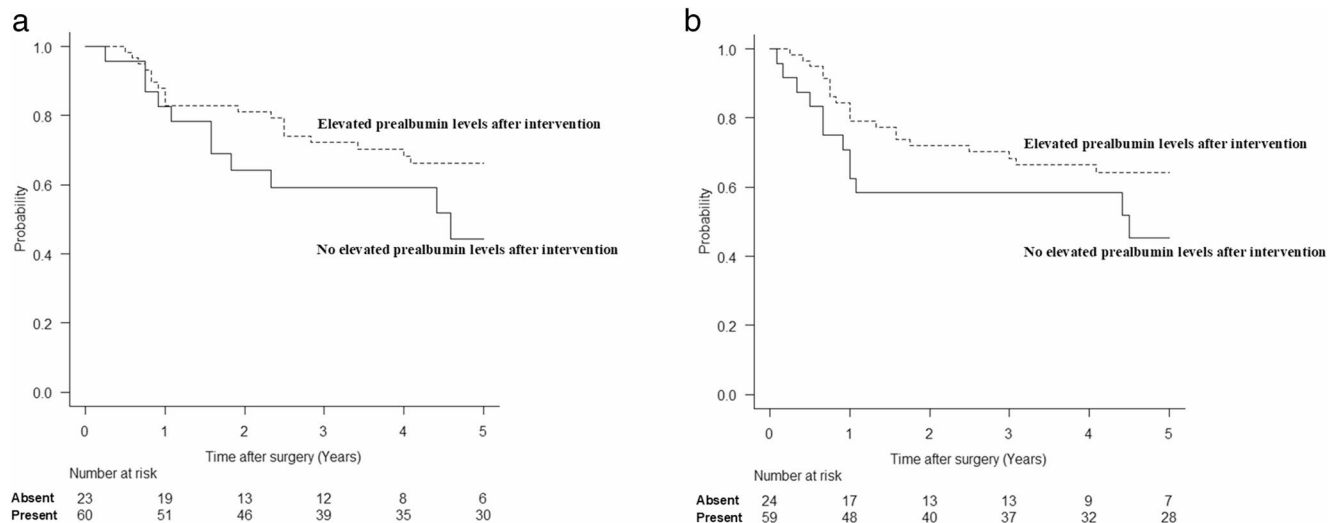


Fig. 4 Comparison of long-term survival in patients with severe malnutrition who underwent nutritional intervention. **a)** Overall survival between groups with elevated prealbumin levels and without elevated

prealbumin levels after intervention **b)** Recurrence-free survival between groups with elevated prealbumin levels and without elevated prealbumin levels after the intervention

were also independent prognostic factors for OS and RFS in multivariate analysis.

One of the problems is that the patients for whom nutritional interventions are provided vary from institution to institution. Therefore, surgery is sometimes performed without sufficient consideration of nutritional status. In fact, about 30% of the patients with GLIM-defined severe malnutrition had no nutritional intervention in this study. One of the reasons for the absence of nutritional intervention was that no consensus was identified on the criteria by which nutritional intervention should be provided.

An index to monitor nutritional improvement in patients who have undergone preoperative nutritional intervention has not yet been clarified. Because changes in body weight and muscle mass take a long time to increase, they are not suitable indicators for the 7–14 days nutritional intervention recommended in the ESPEN guidelines [8, 9]. In addition, albumin has a long half-life as a laboratory value, whereas prealbumin has a short half-life and is expected to be an indicator of nutritional improvement [11–13]. With regard to the cutoff value for prealbumin levels, we have found that an increase of 10% is an indicator of improvement in postoperative complications after gastrectomy [13]. However, patients with low prealbumin levels before intervention meet the definition of 10% or higher as soon as their prealbumin levels rise slightly, suggesting that the variation may be greater depending on what patients are included. We also found that a preoperative prealbumin level < 15 mg/dL was a poor prognostic factor after gastrectomy [12]. However, since patients with malnutrition do not necessarily have low preoperative prealbumin levels, we considered that absolute values are not a good indicator of nutritional improvement

because patients with prealbumin levels ≥ 15 mg/dL before intervention may have prealbumin levels ≥ 15 mg/dL after nutritional intervention without any change in prealbumin levels. Therefore, the definition of nutritional improvement in the absence of a change in the prealbumin level is questionable. The study found that elevated prealbumin levels were prognostically relevant, but the appropriate cutoff values were unclear. A large multicenter prospective study is needed to prove the validity of the cutoff values for prealbumin levels.

A comparison of the groups with and without nutritional intervention revealed that nutritional intervention itself did not prolong long-term survival. This may be because the nutritional intervention group included more patients with advanced cStage and pStage disease. Therefore, the decision to provide nutritional interventions may depend on the selection bias that surgeons consider surgical invasiveness in patients with advanced cancer. This study focused on severely undernourished patients as defined by the GLIM criteria, but still included patients with more advanced cancer in the group with nutritional intervention. Stratified comparisons by pStage showed a favorable prognosis for the group without nutritional intervention in patients with pStage I disease; however, this may be due to the small sample size and unadjusted confounding factors. In contrast, most patients in this study achieved 7–14 days at 30 kcal/kg/day, suggesting that the nutritional intervention was appropriate. Fukuda et al. reported that postoperative infectious complications could be reduced by providing adequate dosage intervention for 10 days or more [18]. Furthermore, they reported no additive effects of nutritional intervention for more than 14 days [18]. Few RCTs have examined the

Table 2 Results of analysis of prognostic factors for overall survival in all patients

Variables	Univariate analysis			Multivariate analysis		
	HR	95%CI	P value	HR	95%CI	P value
Age(years)						
< 70	1			1		
≥ 70	2.227	1.215-4.084	0.010	0.582	0.208-1.627	0.302
Sex						
female	1			1		
Male	1.054	0.626-1.776	0.843	0.970	0.443-2.125	0.940
Preoperative body weight loss						
< 10%	1			1		
≥ 10	0.763	0.451-1.292	0.314	0.453	0.188-1.092	0.078
Surgical procedure						
Distal gastrectomy	1					
Total gastrectomy	0.933	0.523-1.666	0.815	0.499	0.197-1.262	0.142
Surgical approach						
Laparoscopic surgery	1			1		
Open surgery	1.418	0.558-3.602	0.463	0.564	0.061-5.221	0.614
Lymph node dissection						
D1+	1			1		
D2	0.685	0.368-1.276	0.233	0.427	0.139-1.314	0.138
pStage						
I, II	1			1		
III	1.450	0.833-2.523	0.189	3.337	1.218-9.145	0.019
Histological type						
Differentiated	1			1		
Undifferentiated	1.207	0.699-2.084	0.499	2.366	0.907-6.173	0.078
Preoperative CRP						
< 0.5 mg/dL	1			1		
≥ 0.5mg/dL	1.694	0.895-3.207	0.105	1.565	0.663-3.696	0.307
Nutritional intervention						
Absent	1					
Present	1.211	0.663-2.212	0.534			
Elevated prealbumin levels after intervention						
Absent	1			1		
Present	0.624	0.309-1.259	0.188	0.320	0.112-0.917	0.034
Postoperative complication						
Absent	1			1		
Overall complications	1.597	0.896-2.846	0.112	1.805	0.785-4.152	0.165
Adjuvant chemotherapy						
Absent	1			1		
Present	0.377	0.208-0.681	0.001	0.199	0.080-0.496	<0.001

CI confidence interval, CRP C-reactive protein, HR hazard ratio, DG distal gastrectomy, PG proximal gastrectomy, PPG pylorus-preserving gastrectomy, TG total gastrectomy

appropriateness of the duration of administration; therefore, further studies are needed to determine the appropriate duration of nutritional intervention to improve postoperative outcomes.

Multivariate analysis showed that elevated prealbumin levels after nutritional intervention were independent favorable prognostic factors in gastric cancer patients with severe malnutrition. Indicators of nutritional improvement have not been associated with long-term survival. When comparing patient backgrounds between groups with elevated

prealbumin levels and those without elevated prealbumin levels, the group with elevated prealbumin levels had significantly higher prealbumin levels just before surgery, but also included more patients with CRP ≥ 0.5 mg/dL. Prealbumin and albumin levels have been shown to be inversely correlated with CRP levels [11, 19]. However, in this study, the group with elevated prealbumin levels included more patients with mild preoperative inflammation. Merker et al. reported a reduction in 30-day mortality as a result of nutritional intervention using a standard nutritional formula

Table 3 Results of analysis of prognostic factors for recurrence -free survival in all patients

Variables	Univariate analysis			Multivariate analysis		
	HR	95%CI	P value	HR	95%CI	P value
Age(years)						
< 70	1			1		
≥ 70	2.036	1.129-3.671	0.018	0.405	0.140-1.171	0.095
Sex						
Female	1			1		
Male	0.954	0.573-1.590	0.857	0.667	0.302-1.475	0.317
Preoperative body weight loss						
< 10%	1			1		
≥ 10	0.763	0.454-1.282	0.307	0.525	0.227-1.219	0.134
Surgical procedure						
Distal gastrectomy	1			1		
Total gastrectomy	1.019	0.579-1.793	0.948	0.616	0.248-1.531	0.297
Surgical approach						
Laparoscopic surgery	1			1		
Open surgery	1.257	0.534-2.963	0.601	0.407	0.073-2.286	0.307
Lymph node dissection						
D1+	1			1		
D2	0.735	0.396-1.363	0.329	0.375	0.115-1.219	0.103
pStage						
I, II	1			1		
III	1.454	0.846-2.499	0.176	3.321	1.253-8.801	0.016
Histological type						
Differentiated	1			1		
Undifferentiated	1.276	0.743-2.191	0.378	2.687	1.064-6.784	0.037
Preoperative CRP						
< 0.5 mg/dL	1			1		
≥0.5mg/dL	1.026	0.515-2.041	0.943	1.804	0.760-4.279	0.181
Nutritional intervention						
Absent	1			1		
Present	1.151	0.639-2.072	0.640			
Elevated prealbumin levels after intervention						
Absent	1			1		
Present	0.579	0.293-1.146	0.117	0.259	0.094-0.715	0.009
Postoperative complication						
Absent	1			1		
Overall complications	1.501	0.844-2.670	0.166	1.872	0.799-4.387	0.149
Adjuvant chemotherapy						
Absent	1			1		
Present	0.412	0.231-0.734	0.003	0.198	0.078-0.504	<0.001

CI confidence interval, CRP C-reactive protein, HR hazard ratio, DG distal gastrectomy, PG proximal gastrectomy, PPG pylorus-preserving gastrectomy, TG totalgastrectomy

without immunonutrients in patients with inflammation levels < 1–10 mg/dL [20]. Similarly, this study revealed that nutritional intervention using standard nutritional supplements may improve prealbumin levels, even in patients with mild preoperative inflammation. There have been no previous reports on prealbumin cut-off values indicating nutrition and postoperative outcome improvement, making this study significant.

The present study had some limitations. First, this was a single-center, retrospective study. A prospective multicenter

study should be conducted to demonstrate the universality of the cut-off value of prealbumin levels as an indicator of nutritional improvement. It should also be used to demonstrate if improvement of prealbumin levels through nutritional interventions results in improvements in patients' long-term survival. Secondly, the sample size was small. However, despite the small sample size, the effect of elevated prealbumin levels on long-term survival was significant. Third, the mechanism underlying the increase in prealbumin levels after nutritional intervention remains

unclear. Although prealbumin levels are inversely correlated with inflammation, the patients with elevated prealbumin levels included more patients with mild inflammation in this study. Further research, including basic studies, is required to elucidate the mechanism by which prealbumin levels are elevated. Despite these limitations, this is the first study to demonstrate that a measure of nutritional improvement based on prealbumin levels confers improved long-term survival after gastrectomy in patients with gastric cancer and severe malnutrition. The value of this study is very high in that a measure of nutritional improvement based on prealbumin levels can be used in future clinical trials of nutritional interventions.

Conclusion

Preoperative nutritional therapy for patients with severe malnutrition does not contribute to long-term survival after gastrectomy. However, in patients who have undergone preoperative nutritional therapy, prognosis can be predicted by elevated prealbumin levels, potentially becoming a new index for monitoring nutritional interventions. A large, multicenter, prospective study is needed to prove the validity of prealbumin levels and the universality of the results of this study.

Acknowledgements We would like to thank Ms. Ayumi Shimomugi and Dr. Shunsuke Takenaka for data collection, and Dr. Manabu Takamatsu for his advice regarding the pathological findings.

Author contributions All authors contributed to the study's conception and design. Material preparation, data collection, and analysis were performed by RM. The first draft of the manuscript was written by RM and SN and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Funding This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Data availability No datasets were generated or analysed during the current study.

Declarations

Ethics All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Declaration of Helsinki of 1964 and its later versions. Informed consent to be included in the study, or the equivalent, was obtained from all patients. (authorization number: 2022-GB-078).

Informed consent Informed consent was obtained from all individual participants included in the study.

Conflict of interest The authors have no conflicts of interest to declare.

Competing interests The authors declare no competing interests.

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