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Prognostic Importance of Controlling Nutritional Status in Patients Undergoing Curative Thoracoscopic Esophagectomy for Esophageal Cancer

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It is now clear that cancer survival is determined not only by tumor pathology but also by host-related factors, in particular, nutritional status and systemic inflammation. It is desirable that the essential properties of any scale designed or intended to be used for the prediction of survival are simple, convenient, and objective. In this study, we retrospectively reviewed the database of patients who underwent curative surgery for esophageal cancer in our department to evaluate controlling nutritional status (CONUT) and neutrophil–lymphocyte ratio (NLR) as predictors of cancer-specific survival (CSS) after esophagectomy. We retrospectively reviewed the database of 148 consecutive patients who underwent potentially curative surgery for histologically verified esophageal squamous cell carcinoma at our institute between January 2002 and December 2014. CONUT and NLR were calculated. On multivariate analysis, pTNM stage ($P < 0.0001$) and CONUT ($P = 0.0291$) were independently associated with worse prognosis. Multivariate analysis evaluated the prognostic factors in 2 different patient groups: patients younger than 70 years (nonelderly) and those aged 70 years or more (elderly). Multivariate analysis demonstrated that pTNM stage ($P = 0.0083$) and CONUT ($P = 0.0138$) were the independent risk factors for a worse prognosis among the nonelderly group, whereas univariate analysis demonstrated that pTNM stage ($P = 0.0002$) was the only independent risk factor for a worse prognosis among the elderly group. CONUT was a significant predictor of CSS in patients with esophageal cancer in this study. However, pTNM stage remained a significantly more powerful predictor of CSS. Therefore, the results of this study suggested that CONUT and pTNM stage are the significant and complementary factors predicting survival in patients with esophageal cancer. But, this study failed to confirm the NLR as a significant predictor of CSS after resection for esophageal cancer.

Keywords: esophageal cancer, controlling nutritional status, neutrophil–lymphocyte ratio, predictors of cancer-specific survival

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

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INTRODUCTION

The primary curative treatment for esophageal cancer is complete removal of the tumor with esophagectomy, with or without neoadjuvant therapy. Even with potentially curative esophagectomy, however, most patients eventually develop local or distant metastasis, resulting in a poor prognosis.

An elevated preoperative neutrophil-lymphocyte ratio (NLR) has been reported to be an independent prognostic factor with a nearly 2-fold increase in risk for recurrence and death in several cancers. Factors associated with poor overall survival in esophageal cancer include older age, male sex, comorbidities, advanced tumor stage, and poor tumor differentiation.¹

The controlling nutritional status (CONUT) is widely used as an objective index for evaluating nutritional status. CONUT is an efficient tool for the early detection and continuous control of undernutrition in the hospital and also allows assessment of nutritional status in all inpatients.²

CONUT was proposed by Ignacio de Ulíbarri et al and is constructed from laboratory data such as serum albumin, total lymphocyte count, and total cholesterol.² The serum albumin level is used as an indicator of protein reserves. The serum total cholesterol level is used as a parameter of caloric depletion. The total lymphocyte count is used as an indicator of impaired immune defenses due to undernutrition. Therefore, CONUT could be a candidate for a nutritional assessment tool; however, there have been no data available to demonstrate the usefulness of CONUT as a nutritional assessment tool in patients with esophageal cancer.

In this study, we retrospectively reviewed the database of patients who underwent curative surgery for esophageal cancer in our department to evaluate CONUT and NLR as predictors of cancer-specific survival (CSS) after esophagectomy.

PATIENTS AND METHODS

Patients

We retrospectively reviewed the database of 148 consecutive patients with histologically verified esophageal squamous cell carcinoma who underwent potentially curative esophagectomy with R0 resection in our institute, between January 2002 and December 2014. R0 resection was defined as a complete resection without microscopic involvement of margins. Video-assisted or thoracoscopic subtotal esophagectomy with a 3-field lymph node dissection was performed in all patients, followed by laparoscopic gastric surgery with an elevation of the gastric conduit to the neck through the posterior mediastinal pathway or retrosternal pathway with an end-to-end anastomosis of the cervical esophagus and gastric conduit. Patients' clinical characteristics, laboratory data, treatment, and pathological data were obtained from a retrospective review of the records. No patients had clinical signs of infection or other systemic inflammatory conditions preoperatively.

We evaluated the CSS, with the cause of death determined from the case notes or computerized records. Two patients who died within 60 days after esophagectomy were excluded from the analysis.

The definition of elderly patients in this study was being no less than 70 years old. Descriptive statistics were performed in overall patients with esophageal cancer, furthermore, in subgrouped patients to nonelderly (younger than 70 years) or elderly (70 years or older).³

Evaluation of nutritional indices

Laboratory measurements, including the serum levels of C-reactive protein (CRP), albumin, and total cholesterol and the white blood cell count, neutrophil

Table 1. CONUT index score: assessment of dysnutritional state.

Parameter	Dysnutritional state			
	Normal	Mild	Moderate	Severe
Albumin (g/dL)	≥3.50	3.00–3.49	2.50–2.99	<2.50
Score	0	2	4	6
Total lymphocyte count (/mL)	≥1600	1200–1599	800–1199	<800
Score	0	1	2	3
Total cholesterol (mg/dL)	≥180	140–179	100–139	<100
Score	0	1	2	3
Total score	0–1	2–4	5–8	9–12

count, and total lymphocyte count, were performed on the day of admission. As shown in Table 1, the CONUT score was calculated using 3 parameters: serum albumin, total cholesterol level, and total lymphocyte count.² Patients with CONUT scores of 0–1 have a normal nutritional status (CONUT 0), those with CONUT scores of 2–4 are at mild risk of malnutrition (CONUT 1), those with CONUT scores of 5–8 are at moderate risk (CONUT 2), and those with CONUT scores of 9–12 are at severe risk of malnutrition (CONUT 3).

Neutrophil–lymphocyte ratio

The NLR was defined as the absolute neutrophil count divided by the absolute lymphocyte count.⁴ For the purpose of analysis, an NLR of ≥ 3.5 was allocated a score of 1, and a ratio < 3.5 a score of 0.

Definition of margin status and pTNM stage

R0 resection was defined as complete resection without microscopic involvement of margins; R1 was defined as macroscopically complete resection with microscopically involved margins; and R2 was defined as gross residual disease. The pathological classification of the primary tumor, the degree of lymph node involvement, and the presence of organ metastasis were determined according to the pTNM classification system [seventh edition of the American Joint Committee on Cancer (AJCC) Cancer Staging Manual].⁵

Statistical analysis

Mean and SD values were calculated and differences were identified using the Student *t* test. Differences between categories were identified using the χ^2 test.

Table 2. Relationship between CONUT and clinicopathological features in patients with esophageal cancer.

	CONUT 0 (n = 70)	CONUT 1 (n = 62)	CONUT 2–3 (n = 16)	P
Age (yrs)	65.6 \pm 8.2	67.5 \pm 8.4	65.3 \pm 8.9	0.3624
Sex				0.8238
Male	62	55	15	
Female	8	7	1	
CRP (mg/dL)	0.25 \pm 0.32	0.44 \pm 0.89	1.00 \pm 0.94	0.0006
Location of tumor				0.4814
Ce	4	3	3	
Ut	3	6	1	
Mt	32	25	6	
Lt	25	21	6	
Ae	6	7	0	
Tumor size (cm)	3.9 \pm 2.6	4.9 \pm 2.5	4.2 \pm 2.0	0.0937
Depth of tumor				0.0596
pT1a-1b	38	24	3	
pT2	7	4	1	
pT3	21	24	10	
pT4a-4b	4	10	2	
Lymph node metastasis				0.5054
pN0	42	32	7	
pN1	17	20	8	
pN2	6	6	0	
pN3	5	4	1	
Pathological stage				0.0285
p1a-1b	35	19	2	
p2a-2b	14	17	7	
p3a-3c	21	26	7	
Operation time (min)	644.0 \pm 176.5	648.7 \pm 177.9	650.2 \pm 205.5	0.9852
Intraoperative blood loss (mL)	508.9 \pm 467.0	841.7 \pm 751.5	1235.0 \pm 2364.4	0.0127
NLR	2.09 \pm 1.08	2.72 \pm 1.77	4.40 \pm 3.84	<0.0001

CSS curves were produced using the Kaplan–Meier method. Two groups were compared with a 2-sided log-rank test. Hazard ratios were calculated and univariate and multivariate analyses were performed using Cox proportional hazards regression models. The potential prognostic factors for esophageal cancer were as follows: age (<70 vs. ≥70 years), sex (male vs. female), albumin concentration (<3.5 vs. ≥3.5 g/dL), CRP (<1.0 vs. ≥1.0 mg/dL), pT status (pT 1 vs. pT 2–4), pN status (pN 0 vs. pN 1–2); pStage (1, 2 vs. 3), tumor size (<3 vs. ≥3 cm), operation time (<600 vs. ≥600 minutes), intraoperative blood loss (<500 vs. ≥500 mL), CONUT (CONUT 0 vs. CONUT 1–3), and NLR (0 vs. 1). Medical records were retrospectively reviewed to examine these factors.

All statistical analyses were performed using IBM SPSS Statistics version 22 for Windows (IBM Corporation, Armonk, NY), and a *P* value of less than 0.05 was considered statistically significant.

RESULTS

Relationships between CONUT and clinicopathological features in patients with esophageal cancer

Relationships between CONUT and clinicopathological features in 148 patients with esophageal cancer are shown in Table 2. Significant correlations were observed between CONUT and factors such as CRP (*P* = 0.0006), pTNM stage (*P* = 0.0285), intraoperative blood loss (*P* = 0.0127), and NLR (*P* < 0.0001).

Prognostic factors for CSS in patients with esophageal cancer

Univariate analyses demonstrated that the depth of tumor (*P* < 0.0001), lymph node metastasis (*P* < 0.0001), pTNM stage (*P* < 0.0001), tumor size (*P* = 0.0160), operation time (*P* = 0.0298), and CONUT (*P* = 0.0066) were the significant risk factors for a worse prognosis (Table 3).

On multivariate analysis, pTNM stage (*P* < 0.0001) and CONUT (*P* = 0.0291) were independently associated with worse prognosis (Table 3).

Relationships between CONUT and clinicopathological features in nonelderly patients with esophageal cancer

Relationships between CONUT and clinicopathological features in patients younger than 70 years old (nonelderly group) are shown in Table 4. Significant correlations were observed between CONUT and factors such as CRP (*P* = 0.0047), intraoperative blood loss (*P* = 0.0072), and NLR (*P* = 0.0007).

Prognostic factors for CSS in nonelderly patients with esophageal cancer

Among nonelderly patients, univariate analyses demonstrated that the depth of tumor (*P* < 0.0001), lymph node metastasis (*P* = 0.0015), pTNM stage (*P* < 0.0001), tumor size (*P* = 0.0049), and CONUT (*P* = 0.0013) were significantly associated with worse prognosis (Table 5).

Table 3. Prognostic factors for CSS in patients with esophageal cancer.

Variables	Patients (n = 148)	Category or characteristics	Hazard ratio	Univariate		Multivariate		
				95% CI	<i>P</i>	Hazard ratio	95% CI	<i>P</i>
Age (yrs)	96/52	(<70/≥70)	1.659	0.891–3.021	0.1085			
Sex	132/16	(male/female)	0.792	0.360–2.090	0.6070			
CRP (mg/dL)	130/18	(<1.0/≥1.0)	1.505	0.614–3.174	0.3443			
pT	65/83	(1/2, 3, 4)	6.830	3.108–18.009	<0.0001			
pN	80/68	(–/+)	3.282	1.786–6.240	<0.0001			
pStage	94/54	(1, 2/3)	5.246	2.844–10.083	<0.0001	4.348	2.269–8.671	<0.0001
Tumor size (cm)	59/89	(<3.0/≥3.0)	2.175	1.150–4.401	0.0160	1.234	0.627–2.582	0.5518
Operation time (min)	51/97	(<600/≥600)	0.516	0.282–0.937	0.0298	0.631	0.342–1.152	0.1336
Intraoperative blood loss (mL)	63/85	(<500/≥500)	0.983	0.542–1.811	0.9556			
CONUT	70/78	(0/≥1, 2, 3)	2.332	1.259–4.534	0.0066	1.988	1.071–3.875	0.0291
NLR	121/27	(<3.5/≥3.5)	1.368	0.640–2.669	0.3980			

Table 4. Relationship between CONUT and clinicopathological features in nonelderly patients with esophageal cancer.

	CONUT 0 (n = 48)	CONUT 1 (n = 37)	CONUT 2-3 (n = 11)	P
Age (yrs)	61.5 ± 5.4	61.8 ± 5.9	60.4 ± 5.3	0.7686
Sex				0.5249
Male	43	33	10	
Female	5	4	0	
CRP (mg/dL)	0.26 ± 0.35	0.51 ± 1.10	1.16 ± 1.08	0.0047
Location of tumor				0.3002
Ce	3	1	2	
Ut	1	4	0	
Mt	23	18	4	
Lt	15	10	5	
Ae	6	4	0	
Tumor size (cm)	4.1 ± 2.9	4.7 ± 2.7	4.6 ± 2.1	0.5371
Depth of tumor				0.0794
pT1a-1b	26	13	2	
pT2	4	1	1	
pT3	15	15	7	
pT4a-4b	3	8	1	
Lymph node metastasis				0.4384
pN0	31	19	4	
pN1	11	12	6	
pN2	2	3	0	
pN3	4	3	1	
Pathological stage				0.0984
p1a-1b	25	10	2	
p2a-2b	9	10	3	
p3a-3c	14	17	6	
Operation time (min)	664.4 ± 168.1	623.1 ± 144.4	670.4 ± 141.6	0.4346
Intraoperative blood loss (mL)	486.6 ± 472.5	789.9 ± 594.7	1605.5 ± 2805.9	0.0072
NLR	2.11 ± 1.16	2.95 ± 2.15	4.89 ± 4.38	0.0007

Multivariate analysis demonstrated that pTNM stage ($P = 0.0083$) and CONUT ($P = 0.0138$) were the independent risk factors for a worse prognosis (Table 5).

Relationships between CONUT and clinicopathological features in elderly patients with esophageal cancer

Relationships between CONUT and clinicopathological features in patients aged 70 years or above (elderly group) are shown in Table 6. Significant differences were observed between CONUT and tumor size ($P = 0.0086$).

Prognostic factors for CSS in elderly patients with esophageal cancer

Among elderly patients, univariate analyses demonstrated that the depth of tumor ($P = 0.0008$), lymph

node metastasis ($P = 0.0272$), and pTNM stage ($P = 0.0002$) were significantly associated with worse prognosis (Table 7).

Multivariate analyses could not be performed because pTNM is calculated out of the depth of tumor and lymph node metastasis.

Postoperative CSS and CONUT

A significant difference in CSS was seen between overall patients with CONUT of 0 and 1 ($P = 0.049$), but no significant differences in CSS were observed between patients with CONUT of 0 and 2 ($P = 0.063$) or between patients with CONUT of 1 and 2 ($P = 0.139$) (Figure 1A).

In the nonelderly group, there existed significant differences in CSS between patients with CONUT of 0 and 1 ($P = 0.004$) and between patients with CONUT of 0 and 2 ($P = 0.024$), but no significant difference in

Table 5. Prognostic factors for CSS in nonelderly patients with esophageal cancer.

Variables	Patients (n = 96)	Category or characteristics	Univariate			Multivariate		
			Hazard ratio	95% CI	P	Hazard ratio	95% CI	P
Sex	87/9	(male/female)	0.481	0.183–1.650	0.2178			
CRP (mg/dL)	83/13	(<1.0/≥1.0)	1.579	0.527–3.878	0.3822			
pT	41/55	(1/2, 3, 4)	7.851	2.729–33.122	<0.0001			
pN	53/43	(–/+)	3.568	1.619–8.414	0.0015			
pStage	59/37	(1, 2/3)	5.364	2.400–13.101	<0.0001	3.358	1.354–9.090	0.0083
Tumor size (cm)	42/54	(<3.0/≥3.0)	3.334	1.417–9.132	0.0049	1.833	0.696–5.475	0.2282
Operation time (min)	32/64	(<600/≥600)	0.514	0.233–1.122	0.0941			
Intraoperative blood loss (mL)	39/57	(<500/≥500)	1.465	0.666–3.446	0.3482			
CONUT	49/47	(0/≥1, 2, 3)	3.898	1.659–10.665	0.0013	2.955	1.235–8.199	0.0138
NLR	78/18	(<3.5/≥3.5)	1.269	0.335–2.159	0.6177			

CSS was observed between patients with CONUT of 1 and 2 ($P = 0.179$) (Figure 1B).

In the elderly group, no significant differences in CSS were observed between patients with CONUT of 0 and 1 ($P = 0.646$), between patients with CONUT of 0 and 2 ($P = 0.491$), or between patients with CONUT of 1 and 2 ($P = 0.892$) (Figure 1C).

DISCUSSION

Pathological features, including tumor stage, nodal status, and resection margin, are considered to be important in determining survival in patients with cancer.⁶ It is now clear that cancer survival is determined not only by tumor pathology but also by host factors, in particular, nutritional status and systemic inflammation.³ Host-related factors including performance status, weight loss, smoking, and comorbidity, in addition to tumor pathology, play an important role in cancer outcomes.⁷ It is desirable that the essential properties of any scale designed or intended to be used for the prediction of survival are simple, convenient, and objective.

CONUT is constructed from 3 parameters, serum albumin, total lymphocyte count, and total cholesterol. Thus, the CONUT score enables us to evaluate protein reserves (albumin), caloric depletion (total cholesterol), and immune defenses (lymphocyte count). It has become evident that the cancer-associated systemic inflammatory response has an important influence on cancer-related outcomes.^{8,9} Cancer cells recruit inflammatory cells, including neutrophils, which can suppress the action of cytotoxic lymphocytes. Cancer cells themselves may secrete various molecules to induce tumor-facilitating cytotoxic lymphocytes.

Systemic inflammatory responses are associated with alterations in circulating white blood cell counts, leading to neutrophilia and relative lymphopenia.¹⁰ The NLR, a biomarker of the host systemic inflammatory response, has been shown to be highly promising in stratifying outcomes in large cohorts of patients with cancer.¹¹ There have been few reports regarding the prognostic influence of the systemic inflammatory response in esophageal cancers. In this study, we performed an assessment to verify the association of biochemical markers of nutritional status (CONUT) and the systemic inflammatory response (NLR) with CSS in esophageal cancer. In addition, we evaluated the significance of CONUT in both elderly and nonelderly patients with esophageal cancer.

Generally, hypoalbuminemia and hypocholesterolemia are often recognized in elderly populations. The progression of hypoalbuminemia and hypocholesterolemia is likely to be a secondary event after a systemic inflammatory response.^{11–13} CONUT may thus reflect both the presence of an ongoing systemic inflammatory response and the progressive nutritional decline, as shown in the nonelderly patients with esophageal cancer.

Esophageal cancer is often associated with preoperative malnutrition due to mechanical dysphagia. In addition, it has been proposed that increased metabolic demands and the increased production of biological mediators due to advanced tumor stage contribute to malnourishment.

The NLR is an accessible, inexpensive, reproducible, and minimally invasive measure of systemic inflammation that has been investigated as a prognostic marker in a range of solid organ tumors, after cardiovascular diseases.^{14–16} Patients with an elevated NLR have relative lymphocytopenia, which may result in

Table 6. Relationship between CONUT and clinicopathological features in elderly patients with esophageal cancer.

	CONUT 0 (n = 21)	CONUT 1 (n = 26)	CONUT 2–3 (n = 5)	P
Age (yrs)	75.4 ± 3.9	75.2 ± 4.6	76.2 ± 3.1	0.8779
Sex				0.8701
Male	18	23	4	
Female	3	3	1	
CRP (mg/dL)	0.23 ± 0.23	0.32 ± 0.44	0.64 ± 0.44	0.0938
Location of tumor				0.6658
Ce	1	2	1	
Ut	2	2	1	
Mt	8	8	2	
Lt	10	11	1	
Ae	0	3	0	
Tumor size (cm)	3.5 ± 1.7	5.2 ± 2.1	3.3 ± 1.4	0.0086
Depth of tumor				0.6762
pT1a-1b	11	12	1	
pT2	3	3	0	
pT3	6	9	3	
pT4a-4b	1	2	1	
Lymph node metastasis				0.9058
pN0	11	13	3	
pN1	5	9	2	
pN2	4	3	0	
pN3	1	1	0	
Pathological stage				0.1027
p1a-1b	10	9	0	
p2a-2b	4	8	4	
p3a-3c	7	9	1	
Operation time (min)	594.1 ± 192.9	687.7 ± 211.8	605.8 ± 323.5	0.3194
Intraoperative blood loss (mL)	573.3 ± 467.2	892.0 ± 936.5	420.0 ± 273.6	0.2247
NLR	2.07 ± 0.95	2.36 ± 0.90	3.31 ± 2.34	0.0872

a weaker lymphocyte-mediated immune response to the tumor, thereby worsening their prognosis. The NLR has been hypothesized to reflect the balance of the activation of inflammation (neutrophilia) and the cortisol-induced stress response (lymphopenia) in the acute setting, but may also be influenced by the relative lymphopenia of malnutrition.¹⁶ A low lymphocyte count is recognized as a predictor of poor survival in patients with advanced cancer, which is attributed to the role of lymphocytes in cell-mediated immunity causing destruction of cancer cells.¹⁷

There is heterogeneity in the reported thresholds used to define an elevated NLR in the literature. Drawing conclusions based on the use of varied NLR cutoffs is challenging. A significant majority of studies have used a threshold ratio of ≥ 3.5 , and it has been recommended that future work should use this most

commonly used threshold.¹³ In the present study, therefore, we used a threshold of >3.5 . Published data suggest that an elevated preoperative NLR (≥ 3.5) may correlate with an increased risk of recurrence and death in patients who undergo hepatic resection for colorectal liver metastases and for primary hepatocellular carcinoma.^{18,19} It is likely that the mechanisms will be more complex, but NLR is thought to indirectly reflect tumor burden, invasion, and metastasis through the local tumor–host interaction mediated by cytokines and growth factors. In this study, the preoperative NLR did not offer any useful prognostic value in patients who underwent curative esophagectomy. The underlying basis of the relationship between the systemic inflammatory response and poorer cancer survival in patients with esophageal cancer is not clear. Therefore, it is evident that the mechanisms

Table 7. Prognostic factors for CSS in elderly patients with esophageal cancer.

Variables	Patients (n = 52)	Category or characteristics	Univariate			Multivariate		
			Hazard ratio	95% CI	P	Hazard ratio	95% CI	P
Sex	45/7	(male/female)	1.916	0.537–12.202	0.3510			
CRP (mg/dL)	47/5	(<1.0/≥1.0)	1.819	0.284–6.618	0.4651			
pT	24/28	(1/2, 3, 4)	6.241	2.027–27.207	0.0008			
pN	27/25	(–/+))	2.938	1.129–8.176	0.0272			
pStage	35/17	(1, 2/3)	6.229	2.372–17.491	0.0002			
Tumor size (cm)	18/34	(<3.0/≥3.0)	1.152	0.447–3.310	0.7762			
Operation time (min)	19/33	(<600/≥600)	0.540	0.205–1.374	0.1940			
Intraoperative blood loss (mL)	24/28	(<500/≥500)	0.527	0.199–1.352	0.1812			
CONUT	21/31	(0/≥1, 2, 3)	1.128	0.443–2.966	0.8008			
NLR	43/9	(<3.5/≥3.5)	1.729	0.486–4.899	0.3641			

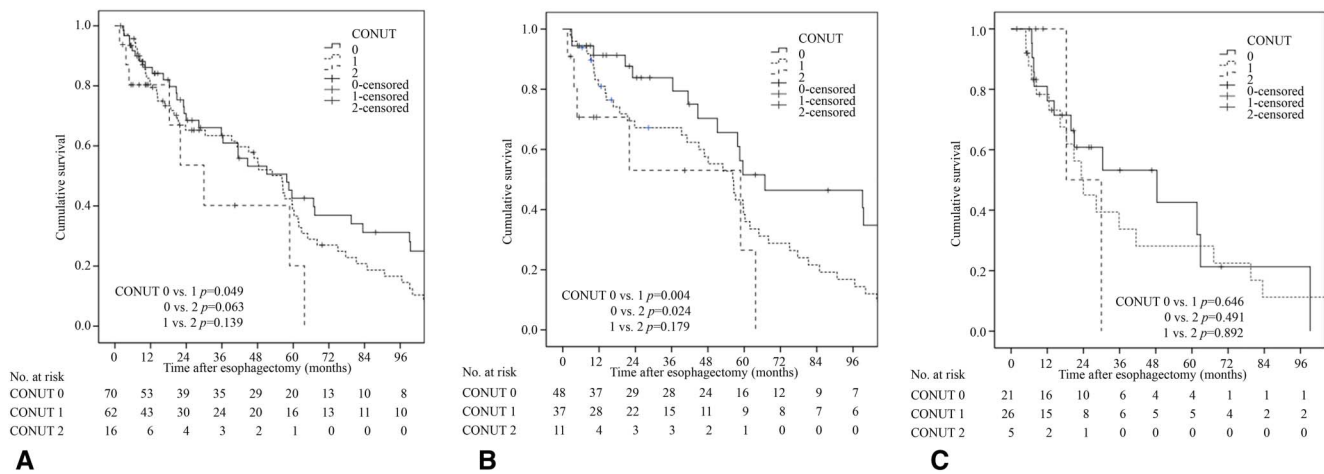


FIGURE 1. Kaplan–Meier survival curves showing the relationship between CONUT levels (CONUT = 0: solid line, CONUT = 1: dotted line, CONUT = 2: dashed line) and CSS after esophagectomy in (A) overall patients with esophageal cancer, (B) nonelderly patients with esophageal cancer, and (C) elderly patients with esophageal cancer.

determining the relationship between CSS and systemic inflammation are complex.

CONUT was a significant predictor of CSS in patients with esophageal cancer in this study. However, pTNM stage remained a significantly more powerful predictor of CSS because the hazard ratio for pTNM stage was 4.348 compared with a hazard ratio of 1.988 for CONUT on multivariate analysis. Therefore, the results of this study suggested that CONUT and pTNM stage are the significant and complementary factors predicting survival in patients with esophageal cancer.

CONUT is easy to measure routinely because of its low cost and convenience, and we found that CONUT is considered to be a useful predictor of postoperative CSS in patients with esophageal cancer. However, there

were several potential limitations in our study. This study was a retrospective study with a small sample size and a short follow-up period, conducted in a single institution. Furthermore, we excluded patients who had received adjuvant chemotherapy and/or radiotherapy, because especially patients who are treated with a neoadjuvant/adjuvant radiochemotherapy suffer from typical side effects such as malnutrition or weight loss. Thus, larger prospective and randomized studies are needed to confirm these preliminary results. Furthermore, the addition of other factors including nutritional indices might improve predictability of the prognosis of esophageal cancer. The potential predictability of other prognostic nutritional scores should be validated prospectively in a multicenter study.

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