in vivo *36*: 1424-1431 (2022)
doi:10.21873/invivo.12847

Clinical Impact of Preoperative Albumin-Bilirubin Status in Esophageal Cancer Patients Who Receive Curative Treatment

TORU AOYAMA[1*], MIHWA JU[1*], DAISUKE MACHIDA[1], KEISUKE KOMORI[1], HIROSHI TAMAGAWA[1], AYAKO TAMAGAWA[1], YUKIO MAEZAWA[1,2], KAZUKI KANO[1], KENTARO HARA[1], KENKI SEGAMI[1], ITARU HASHIMOTO[1], SHINSUKE NAGASAWA[1], MASATO NAKAZONO[1], TAKASHI OSHIMA[1,3], NORIO YUKAWA[1] and YASUSHI RINO[1]

[1]*Department of Surgery, Yokohama City University, Yokohama, Japan;*
[2]*Department of Surgery, Tokyo Metropolitan Cancer and Infectious Diseases Center Komagome Hospital, Tokyo, Japan;*
[3]*Department of Gastrointestinal Surgery, Kanagawa Cancer Center, Yokohama, Japan*

Abstract. *Background/Aim: The albumin-bilirubin (ALBI) score, which evaluates the perioperative liver function, was developed, and had a clinical impact on both the short- and long-term oncological outcomes in some malignancies. We evaluated the clinical impact of preoperative albumin-bilirubin status in patients with resectable esophageal cancer who received curative treatment. Patients and Methods: The study included 121 patients who underwent curative surgery followed by adjuvant chemotherapy for esophageal cancer between 2005 and 2018. The risk factors for overall survival (OS) and recurrence-free survival (RFS) were identified. Results: Based on the 3- and 5-year OS rates, we set the cut-off value for the ALBI score at –2.7. Eighty patients were classified into the ALBI-low group (ALBI score <–2.7), 41 patients were categorized into the ALBI-high group (ALBI score >–2.7). The 3- and 5-year OS rates were 62.2% and 53.2%, respectively, in the ALBI-low group, and 42.2% and 35.2% in the ALBI-high group. There was a significant difference in OS (p=0.0113). The 3- and 5-year RFS rates were 43.1% and 40.3%, respectively, in the ALBI-low group and 37.7% and 26.1% in the ALBI-high group. There was a significant difference in RFS (p=0.048). When comparing the perioperative clinical course between the ALBI-high and ALBI-low groups, the incidence of postoperative anastomotic leakage was 46.3% (19/41) in the ALBI-high group, and 27.5% (22/80) in the ALBI-low group (p=0.038). Conclusion: The ALBI status had a clinical impact on both OS and RFS in esophageal cancer patients. Therefore, ALBI may have potential application as a prognostic factor for esophageal cancer patients.*

In 2012, an estimated 460,000 new esophageal cancer cases and 400,000 deaths occurred worldwide. Esophageal cancer has a 5-year survival rate of <30% and is a major cause of cancer-related death (1, 2). Esophagectomy with lymphadenectomy and perioperative adjuvant therapy is the standard treatment for resectable esophageal cancer (3, 4). Several prognostic factors for resectable esophageal cancer have been reported, including the perioperative nutritional status, metabolic function, and immunological function (5-10). Among them, the liver function is one of the key prognostic factors (11-12). The liver function directly reflects the synthesis and metabolic function of patients (13, 14). On the other hand, there are no optimal methods or tools to evaluate perioperative liver function as a prognostic factor for esophageal cancer.

Recently, the albumin-bilirubin (ALBI) score, which evaluates the perioperative liver function, was developed and has received attention (15). The ALBI score was originally developed to assess the severity of liver function in patients with hepatocellular carcinoma (15). Recent reports showed that the ALBI score had a clinical impact on both the short- and long-term oncological outcomes in some malignancies (16, 17). The ALBI score had clinical advantages over previous methods. It is low cost, easy to measure, and highly reproducible. Recent studies showed that perioperative adjuvant treatment is becoming increasingly important.

*These Authors equally contributed to this study.

Correspondence to: Toru Aoyama, MD, Ph.D., Department of Surgery, Yokohama City University, Yokohama, Japan. Tel: +81 457872800, e-mail: t-aoyama@lilac.plala.or.jp

Key Words: Albumin, bilirubin, esophageal cancer, survival.

Table I. *Comparison of survival rates stratified by patient characteristics.*

Characteristics	No. of patients (%)	1-year OS rate (%)	3-year OS rate (%)	5-year OS rate (%)	*p*-Value
Age (years)					0.2375
<70	86	81.7	59.3	52.5	
≥70	35	74.3	50.9	33.4	
Sex					0.2598
Male	105	78.2	53.7	45.8	
Female	16	86.7	68.1	56.8	
Site of tumor					0.9084
Upper	35	71.4	58.8	58.8	
Middle	52	75.6	48.8	44.3	
Lower	34	87.7	64.3	44.6	
UICC T status					0.0066
T1	42	92.8	74.3	70.4	
T2 to T3	79	72.5	47.8	36.6	
Lymph node metastasis					0.0277
Negative	61	84.8	68.1	59.5	
Positive	60	74.2	45.4	35.9	
Albumin-Bilirubin ratio					0.0113
<–2.7	80	84.6	62.2	53.2	
≥–2.7	41	69.4	42.2	35.2	
Lymph vascular invasion					0.0573
Negative	37	88.7	73.7	62.5	
Positive	84	75.4	49.7	41.2	
Lymph node dissection					0.5678
Two-field	67	80.2	55.2	41.8	
Three-field	54	78.6	56.4	49.3	
Neoadjuvant therapy					0.8595
Yes	54	76.1	56.0	46.6	
No	67	84.2	57.8	48.2	

OS: Overall survival, UICC: Union for International Cancer Control.

Therefore, the evaluation of liver function using the ALBI score is important because the liver function is closely related to the tolerability of adjuvant treatment. However, to our knowledge no studies have evaluated the ALBI score as a prognostic factor in esophageal cancer.

We hypothesized that the preoperative ALBI status may be a potential prognostic factor in esophageal cancer patients. To confirm our hypothesis, we evaluated the clinical impact of the preoperative ALBI status in patients with resectable esophageal cancer who received curative treatment.

Patients and Methods

Patients. Patients were selected based on the medical records of consecutive patients who were diagnosed with primary esophageal adenocarcinoma or squamous cell carcinoma and who underwent complete resection at the Yokohama City University from 2005 to 2018. The inclusion criteria were as follows: 1) stage I-III disease was evaluated according to the 7th edition of the UICC classification, and 2) complete (R0) resection of esophageal cancer with lymphadenectomy, and 3) a laboratory blood analysis was performed within 1 week before surgery. Patients who received R1 or R2 resection were excluded from the present analysis.

Surgical procedure. In principle, subtotal esophagectomy *via* right thoracotomy and reconstruction with a gastric tube was the standard procure. Two-field lymph node dissection was indicated when tumors were located at the middle thoracic to lower thoracic esophagus, while three-field dissection was applied for upper thoracic tumors.

Measurement of the Albumin-Bilirubin (ALBI) Score. The ALBI score was calculated as follows: [ALBI=log10 T-Bil (μmol/l)×0.66+Alb (g/l)×-0.0852]. Data on preoperative blood parameters were extracted from retrospectively collected medical records (15).

Evaluation and statistical analyses. The significance of differences between the ALBI score and clinicopathological parameters was determined using the χ^2 test. The Kaplan-Meier method was used to calculate the overall survival (OS) and recurrence-free survival (RFS) curves. OS was defined as the period between the date of surgery and death. RFS was defined as the period between surgery and the occurrence of an event, recurrence, or death, whichever came first. The data of patients who had not experienced an event were censored at the date of the final observation. The univariate and multivariate survival analyses were performed using a Cox proportional hazards model. *p*-Values <0.05 were considered to indicate statistical significance. The SPSS software program (v26.0 J Win; SPSS,

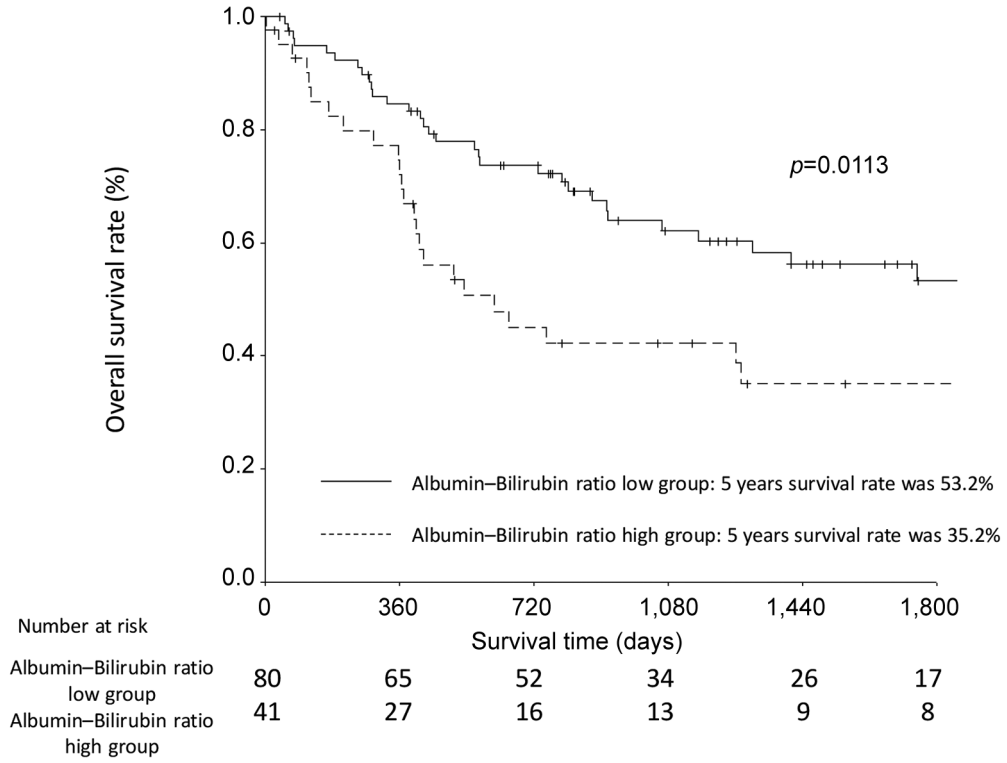

Figure 1. *A comparison of the overall survival of patients in the ALBI-high (ALBI >–2.7) and ALBI-low (ALBI ≤–2.7) groups.*

Chicago, IL, USA) was used for all of the statistical analyses. This study was approved by the IRB of Yokohama City University.

Results

Patients. In the present study, we evaluated 121 patients. The median age was 68 years (range=40-82 years); 104 patients were males, and 16 were females. Based on the 3- and 5-year FOS rate, we set the cut-off value for the ALBI score at –2.7 in the preset study (Table I). Eighty patients were classified into the ALBI-low group (ALBI score <–2.7), while 41 patients were classified into the ALBI-high group (ALBI score >–2.7). When the patient background factors were compared between the ALBI-high group and ALBI-low group, there were not significant differences in the median age (ALBI high *vs*. ALBI low: 66 years *vs*. 67 years, p=0.953), rate of male sex (85% *vs*. 90.2%, p=0.420), smoking habit (90% *vs*. 87.8%, p=0.712), rate of neoadjuvant chemotherapy (53.8% *vs*. 58.5%, p=0.616), incidence of hypertension (41.3% *vs*. 24.3%, p=0.982), incidence of diabetes mellitus (22.5% *vs*. 17.1%, p=0.485), and incidence of chronic pulmonary obstruction (23.8% *vs*. 17.1%, p=0.397).

Survival analyses and patient characteristics. The 3- and 5-year OS rates were 62.2% and 53.2%, respectively, in the ALBI-low group, and 42.2% and 35.2% in the ALBI-high group (Figure 1). There were significant differences in OS (p=0.0113). The clinicopathological factors shown in Table II were analyzed to determine their prognostic significance. In the univariate analyses for OS, that the pathological T status, lymph node metastasis, and ALBI score were significant prognostic factors. The ALBI score was, therefore, selected for the final multivariate analysis model. The 3- and 5-year RFS rates were 43.1% and 40.3%, respectively, in the ALBI-low group, and 37.7% and 26.1% in the ALBI-high group (Figure 2). There were significant differences in RFS (p=0.048). The clinicopathological factors shown in Table III were analyzed to determine their prognostic significance. The univariate analyses for RFS showed that the pathological T status, lymph node metastasis, lymphovascular invasion, and ALBI score were significant prognostic factors. However, the ALBI score was not selected for the final multivariate analysis model. The sites of recurrence in the ALBI-high and ALBI-low groups did not differ to a statistically significant extent (Table IV).

Comparison of perioperative clinical course between ALBI-high group and ALBI-low group. The perioperative clinical course of the ALBI-high and ALBI-low groups was similar. The median postoperative hospital stay, median operative

Table II. *Uni and multivariate Cox proportional hazards analysis of clinicopathological factors for overall survival.*

		Univariate analysis			Multivariate analysis		
Factors	No	OR	95%CI	*p*-Value	OR	95%CI	*p*-Value
Age (years)				0.240			
<70	86	1.000					
≥70	35	1.392	0.802-2.418				
Sex				0.265			
Female	16	1.000					
Male	105	1.685	0.673-4.221				
Site of tumor				0.735			
Middle or Lower	86	1.000					
Upper	35	1.115	0.594-2.091				
UICC T status				0.008			0.084
T1	42	1.000			1.000		
T2 or T3	79	2.359	1.246-4.464		1.810	0.924-3.548	
Lymph node metastasis				0.030			0.096
Negative	61	1.000			1.000		
Positive	60	1.801	1.059-3.063		1.596	0.92-2.764	
Albumin-Bilirubin ratio				0.013			0.042
<–2.7	80	1.000			1.000		
≥–2.7	41	1.946	1.151-3.289		1.750	1.020-3.002	
Lymph vascular invasion				0.061			
Negative	37	1.000					
Positive	84	1.838	0.972-3.477				
Lymph node dissection				0.568			
Two-field	67	1.000					
Three-field	54	1.167	0.687-1.982				
Neoadjuvant therapy				0.860			
Yes	54	1.000					
No	67	1.049	0.617-1.783				

UICC: Union for International Cancer Control.

time, and median intraoperative blood loss were similar. In addition, the incidence of postoperative surgical complications in the ALBI-high and ALBI-low groups was 68.3% (28/41) and 70.0% (56/80), respectively (p=0.847). On the other hand, the incidence of postoperative anastomotic leakage in the ALBI-high and ALBI-low groups was 46.3% (19/41) and 27.5% (22/80), respectively (p=0.038).

Discussion

The aim of the present study was to evaluate the clinical impact of the ALBI status in esophageal cancer patients who received curative treatment. There were two major findings. First, the ALBI status had a clinical impact on both OS and RFS in esophageal cancer patients. Second, the ALBI status was associated with the occurrence of postoperative anastomotic leakage after esophagectomy. Therefore, ALBI may have potential application as a prognostic factor for esophageal cancer patients.

First, we will discuss the clinical impact on the long-term oncological outcome. In the present study, the 3- and 5-year OS rates were 62.2% and 53.2%, respectively, in the ALBI-low group, and 42.2% and 35.2% in the ALBI-high group. Moreover, the hazard ratio (HR) of ALBI for OS was 1.750 (range=1.020-3.002). Similar results were observed in other gastrointestinal cancers reports. Kanda *et al*. evaluated the clinical impact of ALBI in 283 locally advanced gastric cancer who received curative gastrectomy and adjuvant treatment (17). They divided the patients into ALBI-low (n=228) and ALBI-high (n=55) group using a cut-off value of –2.60. They demonstrated that disease-specific survival and disease-free survival were clearly separated according to the ALBI status. The disease-specific survival rate was 66% in the ALBI-high group and 83% in the ALBI-low group (p=0.0014). The disease-free survival rate was 59% in the ALBI-high group and 82% in the ALBI-low group (p=0.0004). Moreover, the ALBI status was a significant prognostic factors for recurrence-free survival (hazard ratio (HR)=1.97, 95% confidence interval (CI)=1.10-3.47, p=0.0242). They concluded that the ALBI grade is a simple and promising predictive factor for disease-free and disease-specific survival of patients with locally advanced gastric

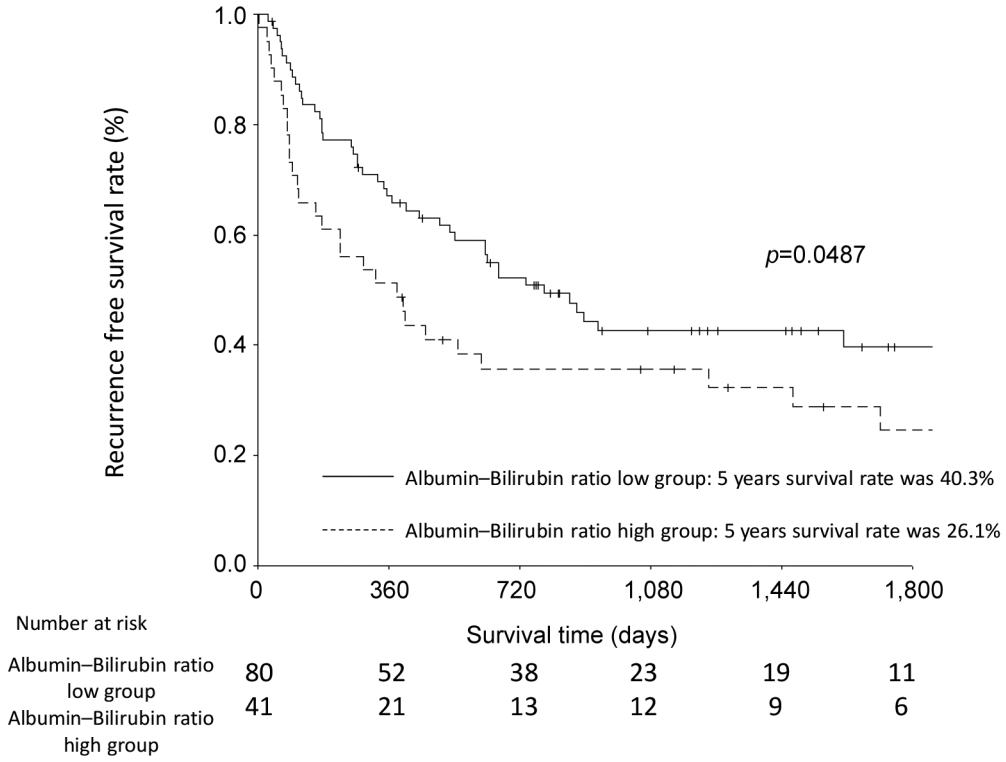

Figure 2. *A comparison of the recurrence-free survival of patients in the ALBI-high (ALBI >–2.7) and ALBI-low (ALBI ≤–2.7) groups.*

cancer. Zhu *et al*. clarified the clinical impact of ALBI in the 243 locally advanced gastric cancer patients who received curative gastrectomy and adjuvant treatment (18). They divided the patients into an ALBI-low group (n=102) and an ALBI-high group (n=141) using a cut-off value of –2.34. When the patient background factors of the ALBI-high and ALBI-low groups were compared, significant differences were observed in BMI, while sex, comorbidity, and tumor stage were almost similar. They demonstrated that overall survival was clearly separated according to ALBI status. Overall survival was 33.8 months in the ALBI-high group and 39.8 months in the ALBI-low group ($p<0.001$). In addition, ALBI was a significant prognostic factor for overall survival (HR=2.3, 95% CI=1.3-4.1, $p=0.005$). Taken together, the ALBI score was considered to be a promising prognostic factor for gastrointestinal cancer patients, including esophageal cancer patients. In addition, the evaluation of the preoperative liver function using the ALBI score may be a useful tool for esophageal cancer patients.

Second, we will discuss the mechanism underlying the association between the ALBI score and long-term oncological outcomes. Why does the ALBI status affect long-term oncological outcomes? There are some possible explanations. First, ALBI showed a significant association with the occurrence of the postoperative anastomotic leakage after esophagectomy. Previously, we demonstrated that postoperative anastomotic leakage after esophagectomy was a prognostic factor in esophageal cancer patients. The 3- and 5-year OS rates were 63.9% and 53.2%, respectively in the non- anastomotic leakage group, and 43.9% and 40.2% in the anastomotic leakage group ($p=0.0049$). Similar results were also reported in previous reports. Zhu *et al*. reported that the ALBI status was associated with the occurrence of postoperative surgical complications (18). They demonstrated that the incidence rates of postoperative surgical complications and severe complications were 32.6% and 11.3%, in the ALBI-high group, and 16.7% and 3.9% in the ALBI-low group ($p=0.005$ and $p=0.038$, respectively). Thus, in esophageal cancer patients, preoperative liver dysfunction may have led to postoperative surgical complications resulting in a poor prognosis. The second possible reason was that the ALBI status may affect adjuvant treatment. Although we could not show the details of the toxicities or the continuation of adjuvant treatment, previous studies showed that ALBI status affected for toxicity or continuation of adjuvant treatment. For example, Miwa *et al*. evaluated the predictive value of the ALBI score for adjuvant treatment in 98 locally advanced gastric cancer patients (19). They divided the patients into an ALBI-high group (n=17) and ALBI-low group (n=81) using a cut-off value of –2.696. They found that

Table III. *Uni and multivariate Cox proportional hazards analysis of clinicopathological factors for recurrence free survival.*

		Univariate analysis			Multivariate analysis		
Factors	No	OR	95%CI	*p*-Value	OR	95%CI	*p*-Value
Age (years)				0.705			
<70	86	1.000					
≥70	35	1.100	0.671-1.805				
Sex				0.280			
Female	16	1.000					
Male	105	1.500	0.719-3.127				
Site of tumor				0.318			
Middle or Lower	86	1.000					
Upper	35	1.334	0.758-2.347				
UICC T status				<0.001			<0.001
T1	42	1.000			1.000		
T2 or T3	79	2.950	1.668-5.217		2.950	1.668-5.217	
Lymph node metastasis				0.013			
Negative	61	1.000					
Positive	60	1.805	1.133-2.878				
Albumin-Bilirubin ratio				0.050			
<–2.7	80	1.000					
≥–2.7	41	1.597	0.998-2.556				
Lymph vascular invasion				0.007			
Negative	37	1.000					
Positive	84	2.182	1.235-3.853				
Lymph node dissection				0.985			
Two-field	67	1.000					
Three-field	54	1.004	0.632-1.596				
Neoadjuvant therapy				0.387			
Yes	54	1.000					
No	67	1.229	0.770-1.959				

UICC: Union for International Cancer Control.

Table IV. *Patterns of recurrence between the patients with Albumin-Bilirubin ratio <–2.70 and those with Albumin-Bilirubin ratio ≥–2.70.*

			Albumin-Bilirubin ratio				
	All cases		<–2.70		≥–2.70		
Recurrence site	Number	%	Number	%	Number	%	*p*-Value
Lymph node							
Regional	23	19.0	18	22.5	5	12.2	0.172
Distant	7	5.8	5	6.3	2	4.9	0.760
Local site	11	9.1	6	7.5	5	12.2	0.395
Distant site							
Lung	14	11.6	12	15.0	2	4.9	0.099
Liver	12	9.9	9	11.3	3	7.3	0.493
Bone	5	4.1	2	2.5	3	7.3	0.208
Others	9	7.4	5	6.3	4	9.8	0.487

the 6-month continuation rate of adjuvant treatment was almost 40% in the ALBI-high group, while it was almost 80% in the ALBI-low group. In addition, a high ALBI score was a risk factor for the discontinuation of adjuvant treatment. They concluded that the preoperative ALBI score was a promising an indicator associated with the tolerability of adjuvant monotherapy in gastric cancer patients. Moreover, Kanda *et al.* also reported similar findings (17). They

demonstrated that the median adjuvant treatment period was 10.7 months in their ALBI-low group and 5.5 months in their ALBI-high group, which amounted to a significant difference (p=0.0437). Accordingly, the ALBI status may have some clinical impact on the continuation of adjuvant treatment. Our future studies will focus on this issue.

Although the ALBI score was a promising tool for the evaluation of the preoperative liver function and a prognostic factor, it is necessary to find the optimal cut-off value for the ALBI score. Previously, the cut-off value was reported to be −2.34 to −2.70. There were several reasons for the differences in the cut-off value. First, the evaluation method to detect the optimal cut-off was different. In the present study, we set the cut-off value according to 3- and 5-year survival rates. On the other hand, other studies used an ROC analysis to determine the optimal cut-off value of the ALBI score. Second, patient background factors and the number of the patients were different. Third, the timing of the evaluation of albumin and bilirubin was different. Considering these factors, further studies should be undertaken to explore the optimal methods and optimal cut-off value of the ALBI score.

In conclusion, the ALBI score had a clinical impact on both OS and RFS in esophageal cancer patients. Therefore, the ALBI score may be applicable as a prognostic factor for esophageal cancer patients and may be a useful tool for decision-making in relation to the treatment of esophageal cancer.

Conflicts of Interest

The Authors declare no conflicts of interest in association with the present study.

Authors' Contributions

Daisuke Machida and Toru Aoyama made substantial contributions to conception and design. Toru Aoyama, Mihwa Ju, Keisuke Komori, Hiroshi Tamagawa, Ayako Tamagawa, Yukio Maezawa, Kazuki Kano, Kentaro Hara, Kenki Segami, Itaru Hashimoto, Shinsuke Nagasawa, Masato Nakazono, Takashi Oshima, Norio Yukawa and Yasushi Rino made substantial contributions to acquisition of data, or analysis and interpretation of data. Daisuke Machida and Toru Aoyama have been involved in drafting the manuscript or revising it critically for important intellectual content. Daisuke Machida and Toru Aoyama have given final approval of the version to be published. Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content; and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All Authors read and approved the final manuscript.

References

1 Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J and Jemal A: Global cancer statistics, 2012. CA Cancer J Clin *65(2)*: 87-108, 2015. PMID: 25651787. DOI: 10.3322/caac.21262

2 Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA and Jemal A: Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin *68(6)*: 394-424, 2018. PMID: 30207593. DOI: 10.3322/caac.21492

3 Lordick F, Mariette C, Haustermans K, Obermannová R, Arnold D and ESMO Guidelines Committee: Oesophageal cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol *27(suppl 5)*: v50-v57, 2016. PMID: 27664261. DOI: 10.1093/annonc/mdw329

4 Muro K, Lordick F, Tsushima T, Pentheroudakis G, Baba E, Lu Z, Cho BC, Nor IM, Ng M, Chen LT, Kato K, Li J, Ryu MH, Zamaniah WIW, Yong WP, Yeh KH, Nakajima TE, Shitara K, Kawakami H, Narita Y, Yoshino T, Van Cutsem E, Martinelli E, Smyth EC, Arnold D, Minami H, Tabernero J and Douillard JY: Pan-Asian adapted ESMO Clinical Practice Guidelines for the management of patients with metastatic oesophageal cancer: a JSMO-ESMO initiative endorsed by CSCO, KSMO, MOS, SSO and TOS. Ann Oncol *30(1)*: 34-43, 2019. PMID: 30475943. DOI: 10.1093/annonc/mdy498

5 Chen SB, Liu DT and Chen YP: The impact of preoperative nutritional status on the survival of patients with esophageal squamous cell carcinoma. Front Surg *8*: 752792, 2021. PMID: 34988110. DOI: 10.3389/fsurg.2021.752792

6 Yago A, Ohkura Y, Ueno M, Fujisawa K, Ogawa Y, Shimoyama H, Urabe M, Haruta S and Udagawa H: Identification of preoperative fat-free mass index for the prognosis of curatively resected esophageal cancer. World J Surg *46(4)*: 845-854, 2022. PMID: 34985544. DOI: 10.1007/s00268-021-06435-3

7 Wiwitkeyoonwong J, Jiarpinitnun C, Hiranyatheb P and Ngamphaiboon N: Impact of weight loss on patients with locally advanced esophageal and esophagogastric junction cancers treated with chemoradiotherapy. Asian Pac J Cancer Prev *22(12)*: 3847-3855, 2021. PMID: 34967563. DOI: 10.31557/APJCP.2021.22.12.3847

8 Li S, Qiu R, Yuan G, Wang Q, Li Z, Li Q and Zhang N: Body composition in relation to postoperative anastomotic leakage and overall survival in patients with esophageal cancer. Nutrition *94*: 111534, 2022. PMID: 34952360. DOI: 10.1016/j.nut.2021.111534

9 Yoon JP, Nam JS, Abidin MFBZ, Kim SO, Lee EH, Choi IC and Chin JH: Comparison of preoperative nutritional indexes for outcomes after primary esophageal surgery for esophageal squamous cell carcinoma. Nutrients *13(11)*: 4086, 2021. PMID: 34836339. DOI: 10.3390/nu13114086

10 Atsumi Y, Kawahara S, Kakuta S, Onodera A, Hara K, Kazama K, Numata M, Aoyama T, Tamagawa A, Tamagawa H, Oshima T, Yukawa N and Rino Y: Low preoperative albumin-to-globulin ratio is a marker of poor prognosis in patients with esophageal cancer. In Vivo *35(6)*: 3555-3561, 2021. PMID: 34697194. DOI: 10.21873/invivo.12658

11 Valmasoni M, Pierobon ES, De Pasqual CA, Zanchettin G, Moletta L, Salvador R, Costantini M, Ruol A and Merigliano S: Esophageal cancer surgery for patients with concomitant liver cirrhosis: a single-center matched-cohort study. Ann Surg Oncol *24(3)*: 763-769, 2017. PMID: 27704371. DOI: 10.1245/s10434-016-5610-8

12 Asti E, Sozzi M, Bonitta G, Bernardi D and Bonavina L: Esophagectomy in patients with liver cirrhosis: a systematic review and Bayesian meta-analysis. J Visc Surg *155(6)*: 453-464, 2018. PMID: 29653854. DOI: 10.1016/j.jviscsurg.2018.03.014

13 Jones JG: Hepatic glucose and lipid metabolism. Diabetologia *59(6)*: 1098-1103, 2016. PMID: 27048250. DOI: 10.1007/s00125-016-3940-5

14 Han HS, Kang G, Kim JS, Choi BH and Koo SH: Regulation of glucose metabolism from a liver-centric perspective. Exp Mol Med *48*: e218, 2016. PMID: 26964834. DOI: 10.1038/emm.2015.122

15 Johnson PJ, Berhane S, Kagebayashi C, Satomura S, Teng M, Reeves HL, O'Beirne J, Fox R, Skowronska A, Palmer D, Yeo W, Mo F, Lai P, Iñarrairaegui M, Chan SL, Sangro B, Miksad R, Tada T, Kumada T and Toyoda H: Assessment of liver function in patients with hepatocellular carcinoma: a new evidence-based approach-the ALBI grade. J Clin Oncol *33(6)*: 550-558, 2015. PMID: 25512453. DOI: 10.1200/JCO.2014.57.9151

16 Imamura T, Okamura Y, Sugiura T, Ito T, Yamamoto Y, Ashida R, Ohgi K, Otsuka S and Uesaka K: Clinical significance of preoperative albumin-bilirubin grade in pancreatic cancer. Ann Surg Oncol *28(11)*: 6223-6235, 2021. PMID: 33486645. DOI: 10.1245/s10434-021-09593-9

17 Kanda M, Tanaka C, Kobayashi D, Uda H, Inaoka K, Tanaka Y, Hayashi M, Iwata N, Yamada S, Fujii T, Sugimoto H, Murotani K, Fujiwara M and Kodera Y: Preoperative albumin-bilirubin grade predicts recurrences after radical gastrectomy in patients with pT2-4 gastric cancer. World J Surg *42(3)*: 773-781, 2018. PMID: 28920160. DOI: 10.1007/s00268-017-4234-x

18 Zhu C, Wang X, Chen S, Yang X, Sun J, Pan B, Zhang W, Chen X and Huang Y: Efficacy of the preoperative albumin-bilirubin grade for predicting survival and outcomes of postoperative chemotherapy for advanced gastric cancer. Cancer Manag Res *12*: 11921-11932, 2020. PMID: 33244269. DOI: 10.2147/CMAR.S279782

19 Miwa T, Kanda M, Tanaka C, Kobayashi D, Hayashi M, Yamada S, Nakayama G, Koike M and Kodera Y: Albumin-bilirubin score predicts tolerability to adjuvant S-1 monotherapy after curative gastrectomy. J Gastric Cancer *19(2)*: 183-192, 2019. PMID: 31245163. DOI: 10.5230/jgc.2019.19.e15

Received February 3, 2022
Revised February 25, 2022
Accepted March 23, 2022