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Albumin and Neutrophil-to-Lymphocyte Ratio Score in Neoadjuvant Concurrent Chemoradiotherapy for Esophageal Cancer: Comparison With Prognostic Nutritional Index

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Abstract. *Background/Aim: Neoadjuvant concurrent chemoradiotherapy (CCRT) for esophageal cancer is often overwhelming due to its toxic effects. This study aimed to establish a prognostic indicator based on pretreatment albumin and neutrophil-to-lymphocyte (NLR) ratio score (ANS) in comparison to the Prognostic Nutritional Index (PNI) in patients with esophageal cancer. Patients and Methods: A total of 123 patients who received neoadjuvant CCRT for esophageal cancer were prospectively and consecutively recruited between August 2016 and December 2017 from three medical institutes in Taiwan. Patients were assigned to ANS 0, 1, and 2 groups based on their pretreatment albumin and NLR values. ANS and PNI performances were compared for prediction of survival outcome. Results: Compared with ANS 0 (39 patients) and ANS 1 (51 patients), ANS 2 (33 patients) cases showed worse overall survival (hazard ratio=2.96; 95% confidence interval=1.45-6.05; log-rank p=0.003; hazard ratio=3.79; 95% confidence interval=1.79-8.02, p<0.001, respectively). ANS had better performance in overall survival evaluation and discrimination ability than PNI and individual albumin and NLR. Patients in the ANS 0, 1, and 2 had radiotherapy incompletion rates of 2.6%, 3.9%, and 18.2%, respectively, and chemotherapy incompletion rates of 5.1%, 7.8%, and 30.3%, respectively. Patients in the ANS 2 group were significantly associated with a higher incidence of infection (30.3%) than those in the ANS 0 (10.3%) and ANS 1 groups (9.8%). Conclusion: Pre-treatment ANS was significantly associated with CCRT safety profiles, CCRT completion rate, and survival outcome in patients with esophageal cancer with excellent performance compared to PNI and NLR.*

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As of 2020, esophageal cancer is the 10th most common cancer and 6th leading cause of cancer-related deaths worldwide. Owing to its insidious nature, patients with esophageal cancer are often diagnosed during locally advanced stages at the time of presentation, deeming upfront primary resection unfeasible (1). The goal of neoadjuvant concurrent chemoradiotherapy (CCRT) is to downstage the tumors for a greater chance of complete resection. Although neoadjuvant CCRT improved the survival outcome of the majority of patients, a substantial number of patients may be overwhelmed by its toxic effect, which results in premature termination of treatment or death from CCRT-related side effects.

While CCRT followed by surgery demonstrated an increase in overall survival (OS) in locally advanced esophageal cancer, there is a lack of a reliable predictive factor to identify patients who are more likely to be overwhelmed by CCRT side effects (2). As predictive factors become more accurate, treatments may become more tailored for individual patients to minimize treatment-related adverse events without compromising survival outcomes.

Albumin and neutrophil-to-lymphocyte ratio (NLR) are surrogate markers for the evaluation of patients' nutrition and

inflammation level (3). Albumin is the most abundant plasma protein found in humans. A lower albumin level indicates malnourishment or is associated with an inflammatory process that inhibits albumin production or increases consumption of albumin (4). The NLR is defined as the absolute number of neutrophils divided by the absolute number of lymphocytes. Increased numbers of neutrophils and/or decreased numbers of lymphocytes may suppress lymphokine-activated killer cells, suggesting an increased propensity for tumor growth. While albumin and NLR values are both cost-effective and easily evaluated in clinical practice, studies have evaluated low levels of these factors individually to be associated with poor treatment outcomes in patients with esophageal cancer (5). Although malnutrition and inflammation are common conditions in patients with esophageal cancer (6), the combination of the two, also known as the albumin NLR score (ANS) (7), has not been thoroughly evaluated as a predictor of treatment outcomes in esophageal cancer patients who underwent CCRT.

This study aimed to evaluate the effectiveness of ANS as a predictive and prognostic tool for predicting survival outcomes, treatment-related adverse events, and treatment completion rates in patients undergoing CCRT for locally advanced esophageal cancer.

Patients and Methods

Patient selection. This prospective observational study investigated the effectiveness and safety profiles of neoadjuvant CCRT in patients with locally advanced esophageal cancer. A total of 123 patients were consecutively recruited between August 2016 and December 2017 from three medical institutes in Taiwan. Eligibility criteria included patients aged 20 years or older with histologically proven esophageal cancer who were eligible for CCRT as the first-line antitumor treatment. A locally advanced tumor was defined as any non-metastatic tumor from the cervical esophagus, ≥T2 classification, or any regional node-positive tumor. Exclusion criteria included metastatic disease, inability to provide informed consent for any reason, and treatment with chemotherapy or radiotherapy alone. Tumor staging was performed according to the 7th edition of the American Joint Committee on Cancer (AJCC) staging system. The study protocol was approved by the institutional review board (no. 1608080002).

Concurrent chemoradiation therapy. All eligible patients received either CCRT with PF (cisplatin 100 mg/m^2 and 5-fluorouracil 1,000 mg/m^2/d for 4 days in weeks 1 and 5, concurrent with radiotherapy 1.8 Gy×28 fractions for a total of 50.4 Gy) (8) or Pac/Car (paclitaxel 50 mg/m^2 and carboplatin area under the curve of 2 mg/ml/min day 1 weekly over 5 weeks, concurrent with radiotherapy 1.8 Gy×23 fractions for a total of 41.4 Gy) (9). Tumor restaging was assessed with computed tomography (CT) and esophagogastroduodenoscopy (EGD) within 4 weeks after the completion of radiotherapy. After the completion of treatment, the resectability of the tumor was evaluated using a specialized tumor board, based on the response of the tumors and the clinical condition of the patients. The patients underwent minimally invasive transthoracic esophagectomy (Ivor-Levis) with mediastinal lymphadenectomy within 4-8 weeks after the completion of CCRT, if the residual tumor was deemed resectable by the board. Local booster radiotherapy at 2,340 cGy was administered to the tumor bed and regional lymphatic area over 13 fractions in patients who did not undergo surgical resection or those with positive pathological lymph node metastases after surgery.

Albumin and neutrophil-lymphocyte-ratio score. The patients' demographic and clinicopathological data at the onset of CCRT treatment were obtained. Laboratory data were obtained within seven days before the initiation of CCRT. An NLR value less than or higher than the median (3.1 in this study) was assigned to 0 and 1 point, respectively, whereas an albumin value higher or lower than the median (4.1 g/dl) was assigned to 0 and 1 point, respectively (7). Accordingly, patients were assigned to ANS 0, 1, and 2 groups based on their albumin and NLR values.

Prognostic nutritional index. The prognostic nutritional index (PNI) was calculated using the following formula: 10×serum albumin value (g/dl)+0.005×total lymphocyte count in peripheral blood (per mm^3). Our study used the cutoff point 45 for PNI for comparison, according to the previous study (10).

Survival outcome and adverse events evaluation. The OS time was determined from the date of CCRT until death or until the last date on which the patient was known to be alive. The patients' grades for any adverse event were evaluated at least weekly during CCRT. Treatment-related toxicities were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events, version 3.0. All adverse events were recorded from CCRT initiation until 1 month after the end of CCRT.

Statistical analysis. Basic patient demographic data are summarized as frequency (%) for categorical variables and as median with interquartile range (IQR) or range for continuous variables. Differences in tumor response between the three ANS groups were compared using the chi-square (χ^2) test.

Survival outcomes were calculated using the Kaplan-Meier method. Log-rank tests were used to determine significant differences between survival curves. A Cox regression model was used to estimate the hazard ratio (HR) for the variables associated with OS.

To compare the performance of the model, linear chi-square test, -2 log likelihood, and c-index were used. In general, a higher linear chi-squared and lower -2 log likelihood values indicate a more accurate model, and a higher c-index value indicates an increased discriminative ability of the model. SPSS software (version 17.0; SPSS Inc., Chicago, IL, USA) was used for all the statistical analyses. All statistical assessments were 2-sided and a p-value of <0.05 was considered the threshold for statistical significance.

Results

The basic characteristics of the 123 patients included in this study are presented in Table I. The median patient age was 56 years (range=28-82 years), and 92.7% of the patients were male. The most common histological type was squamous cell carcinoma (97.6%). Most patients (66.7%)

Table I. *Patient characteristics*.

Variable	Overall (n=123)	ANS 0 (n=39)	ANS 1 (n=51)	ANS 2 (n=33)	*p*-Value
Median age, years (range)	56 (28-82)	55 (48-69)	57 (28-82)	56 (36-77)	0.78
Sex, n (%)					0.51
Male	114 (92.7)	36 (92.3)	46 (90.2)	32 (97.0)	
Female	9 (7.3)	3 (7.7)	5 (9.8)	1 (3.0)	
Education, n (%)					0.64
Nil/elementary	31 (25.2)	8 (20.5)	12 (23.5)	11 (33.3)	
Junior high school	50 (40.7)	15 (38.5)	23 (45.1)	12 (36.4)	
Senior high school or higher	42 (34.1)	16 (41.0)	16 (31.4)	10 (30.3)	
Marriage, n (%)					0.19
Yes	95 (77.2)	32 (82.1)	38 (74.5)	25 (75.8)	
No	28 (22.8)	7 (17.9)	13 (25.5)	8 (24.2)	
Occupation, n (%)					0.98
Yes	90 (73.2)	10 (25.6)	14 (27.5)	9 (27.3)	
No	22 (26.8)	29 (74.4)	37 (72.5)	24 (72.7)	
Alcohol consumption, n (%)					0.38
No	8 (6.5)	1 (2.6)	5 (9.8)	2 (6.1)	
Yes	115 (93.5)	38 (97.4)	46 (90.2)	31 (93.9)	
Cigarette smoking, n (%)					0.06
No	6 (4.9)	0	2 (3.9)	4 (12.1)	
Yes	117 (95.1)	39 (100)	49 (96.1)	29 (87.9)	
Betel-quid chewing, n (%)					0.98
No	33 (26.8)	10 (25.6)	14 (27.5)	9 (27.3)	
Yes	90 (73.2)	29 (74.4)	37 (72.5)	24 (72.7)	
Body mass index, kg/m^2, median (range)	21.8 (15.9-31.6)	22.7 (18.3-31.0)	22.0 (16.9-31.6)	20.8 (15.9-27.3)	0.002
ECOG performance, n (%)					<0.001
0	64 (52.0)	31 (79.5)	24 (47.1)	9 (27.3)	
1	57 (46.3)	8 (20.5)	27 (52.9)	22 (66.7)	
2	2 (1.6)	0	0	2 (6.1)	
Charlson comorbidity index, n (%)					0.011
0	59 (48.0)	26 (66.7)	22 (43.1)	11 (33.3)	
1	30 (24.4)	9 (23.1)	14 (27.5)	7 (21.2)	
≥2	34 (27.6)	4 (10.3)	15 (29.4)	15 (45.5)	
Histological type, n (%)					0.21
Squamous cell carcinoma	120 (97.6)	38 (97.4)	51 (100)	31 (93.9)	
Adenocarcinoma	3 (2.4)	1 (2.6)	0	2 (6.1)	
Tumor location, n (%)					0.14
Upper	22 (17.9)	7 (17.9)	12 (23.5)	3 (9.1)	
Middle	43 (35.0)	12 (30.8)	20 (39.2)	11 (33.3)	
Lower	31 (25.2)	14 (35.9)	10 (19.6)	7 (21.2)	
Overlapping	27 (22.0)	6 (15.4)	9 (17.6)	12 (36.4)	
Tumor length, cm, median (range)	5.0 (1.0-17.0)	5.0 (1.9-15.0)	5.0 (1.0-10.5)	6.8 (2.0-17.0)	0.001
Tumor stage, n (%)					0.12
2	23 (18.7)	11 (28.2)	9 (17.6)	3 (9.1)	
3	82 (66.7)	26 (66.7)	33 (64.7)	23 (69.7)	
4a	18 (14.6)	2 (5.1)	9 (17.6)	7 (21.2)	
Chemotherapy regimen, n (%)					0.84
Carboplatin+paclitaxel	76 (61.8)	25 (64.1)	32 (62.7)	19 (57.6)	
Cisplatin+5-fluorouracil	47 (38.2)	14 (35.9)	19 (37.3)	14 (42.4)	
Post-CCRT operation, n (%)					0.008
Yes	46 (37.4)	21 (53.8)	19 (37.3)	6 (18.2)	
No	77 (62.6)	18 (46.2)	32 (62.7)	27 (81.8)	
PNI, median (range)	50.9 (25.3-69.7)	55.8 (50.1-69.7)	50.4 (37.4-58.7)	43.1 (25.3-51.5)	<0.001

ECOG: Eastern Cooperative Oncology Group; CCRT: concurrent chemoradiotherapy; PNI: Prognostic Nutritional Index.

had stage III disease, and 61.8% of all patients received carboplatin plus paclitaxel as a chemotherapeutic regimen for CCRT.

In total, 39 (31.7%), 51 (41.5%), and 33 (26.8%) patients were allocated to ANS 0, 1, and 2 groups, respectively. No statistical differences were observed among the different ANS

Table II. *Univariate and multivariate analysis for overall survival.*

Variable	Category	Univariate analysis		Multivariate analysis	
		HR (95%CI)	*p*-Value	Adjusted HR (95%CI)	*p*-Value
Age, years	≥55	1			
	<55	0.94 (0.58-1.55)	0.82		
Sex	Male	1			
	Female	0.97 (0.39-2.42)	0.97		
Education	Nil/elementary	1			
	Junior high school	1.13 (0.60-2.12)	0.70		
	Senior high school or higher	0.87 (0.44-1.69)	0.67		
Cigarette smoking	No	1			
	Yes	1.20 (0.48-3.01)	0.67		
Alcohol consumption	No	1			
	Yes	1.43 (0.52-4.00)	0.49		
Betelnut chewing	No	1			
	Yes	1.15 (0.66-1.96)	0.63		
Charlson comorbidity index	0	1			
	1	1.10 (0.60-2.03)	0.75		
	≥2	1.11 (0.2-2.00)	0.72		
Body mass index, kg/m^2	<22	1			
	≥22	0.95 (0.58-1.56)	0.54		
ECOG performance	0	1		1	
	1	2.40 (1.43-4.03)	0.001	1.59 (090-2.85)	0.11
	2	4.22 (0.99-18.1)	0.052	1.53 (0.30-7.89)	0.61
Histological type	Adenocarcinoma	1			
	Squamous cell carcinoma	1.25 (0.31-5.13)	0.75		
Tumor location	Upper	1			
	Middle	1.23 (0.59-2.57)	0.58		
	Lower	1.02 (0.46-2.26)	0.96		
	Overlapping	1.05 (0.46-2.38)	0.92		
Tumor stage	2	1		1	
	3	2.17 (0.97-4.82)	0.058	2.50 (1.09-5.73)	0.031
	4a	4.29 (1.70-10.8)	0.002	2.74 (1.04-7.27)	0.042
Surgical resection	No	1		1	
	Yes	0.36 (0.20-0.64)	<0.001	0.48 (0.25-0.91)	0.024
Chemotherapy regimen	Cisplatin+5-fluorouracil	1		1	
	Carboplatin+paclitaxel	0.49 (0.30-0.80)	0.005	0.57 (0.34-0.95)	0.031
Albumin, gm/dl	≥4.1	1			
	<4.1	1.30 (1.01-2.12)	0.038		
NLR	<3.1	1			
	≥3.1	2.13 (1.38-3.29)	0.001		
PNI	≥45	1			
	<45	1.62 (1.00-2.62)	0.048		
ANS	0	1		1	
	1	2.96 (1.45-6.05)	0.003	1.74 (1.01-4.47)	0.046
	2	3.79 (1.79-8.02)	<0.001	2.15 (1.04-4.56)	0.017

ECOG: Eastern Cooperative Oncology Group; NRL: neutrophil-to-lymphocyte ratio; PNI: Prognostic Nutritional Index; ANS: albumin-NLR score.

groups in terms of age, sex, marital status, education, occupation, smoking, alcohol consumption, betel quid chewing, histological type, tumor location, tumor stage, and chemotherapeutic agents. Patients in the ANS 2 group had a lower body mass index, poorer ECOG performance status, higher tumor length, lower PNI value, and were less likely to undergo surgical resection after CCRT than those in the other two ANS groups.

The median follow-up was 22.0 months (range=1.9-31.8 months), and 67 patients (49.3%) died at the end of the follow-up. In the univariate analysis (Table II), ECOG performance, tumor stage, surgical resection, chemotherapeutic regimen, albumin, NLR, PNI, and ANS were significant factors for OS. To avoid the interaction of albumin, NLR, PNI, and ANS, only ANS (variable with the

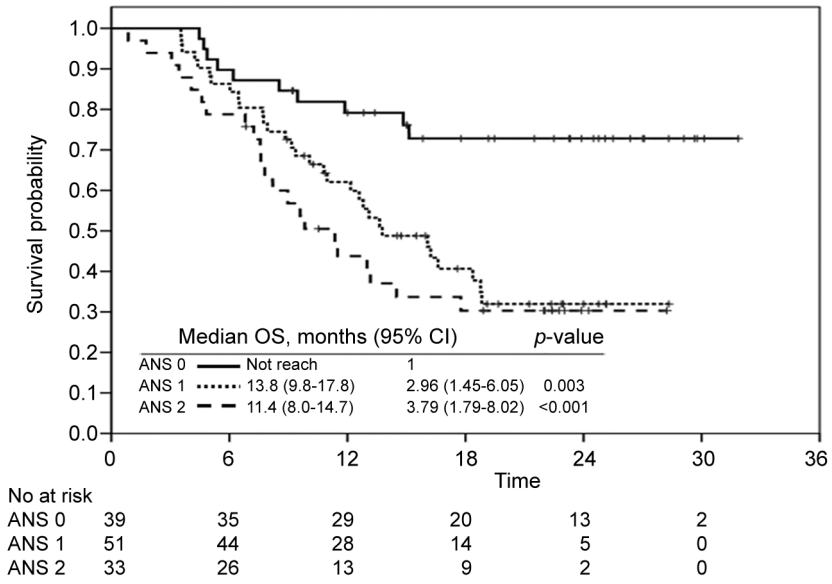

Figure 1. *Survival outcome according to albumin and neutrophil-to-lymphocyte ratio score (ANS) groups. OS: Overall survival; HR: hazard ratio; CI: confidence interval.*

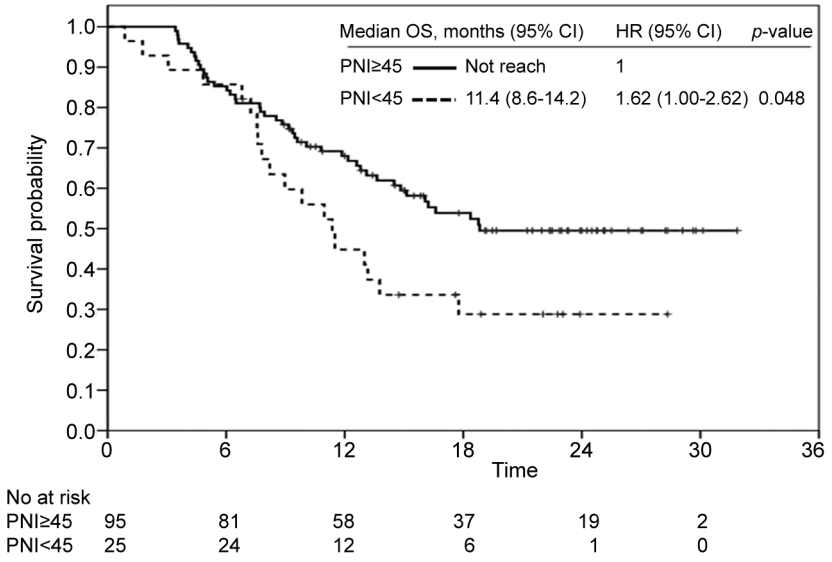

Figure 2. *Survival outcome according to Prognostic Nutritional Index (PNI) groups. OS: Overall survival; HR: hazard ratio; CI: confidence interval.*

highest chi-square value) was included in the multivariate analysis. Tumor stage, surgical resection, chemotherapeutic regimen, and ANS were independent prognostic factors in the multivariate analysis.

The subgroup survival curves of patients in the different albumin, NLR, ANS, and PNI groups are shown in Figure 1. The chemotherapy and radiotherapy completion rates stratified by ANS score are shown in Figure 2. ANS 0, 1, and 2 had radiotherapy incompletion rates of 2.6%, 3.9%, and 18.2%, respectively. ANS 0, 1, and 2 had chemotherapy incompletion rates of 5.1%, 7.8%, and 30.3%, respectively. Figure 3 shows the surgical resection rates after CCRT, according to the ANS. ANS 0, 1, and 2 had surgical resection rates of 53.8%, 37.3%, and 18.2%, respectively, after CCRT. A significant survival difference was observed among patients in the albumin, NLR, ANS, and PNI groups. Table III shows the predictive performance of CCRT incompleteness for albumin level, NRL, ANS, and PNI. The

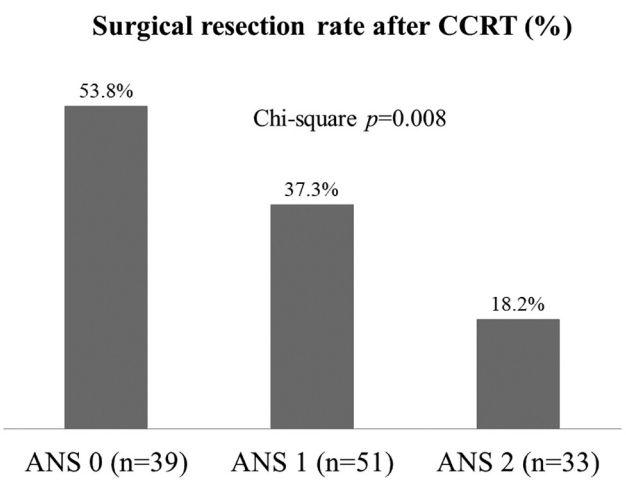

Figure 3. *Surgical resection rate after concurrent chemoradiotherapy according to albumin and neutrophil-to-lymphocyte ratio score (ANS) groups. CCRT: Neoadjuvant concurrent chemoradiotherapy.*

Table III. *Survival predicting performance among albumin, neutrophil-to-lymphocyte ratio (NLR), and albumin-NLR score (ANS).*

Model	Chi-square*	Likelihood ratio**	C-index (95%CI)***
Albumin	6.50	7.89	0.568 (0.462-.674)
NLR	9.94	8.17	0.639 (0.538-0.741)
PNI	4.38	6.32	0.624 (0.517-0.731)
ANS	14.1	15.7	0.651 (0.551-0.751)

CI: Confidence interval; PNI: Prognostic Nutritional Index. *A higher chi-square value of linear trend indicates a better discriminatory ability and gradient monotonicity of the model. **A higher likelihood ratio value indicates a smaller difference within the model and is an indicator of better homogeneity. ***A higher c-index means a better discriminatory ability of the model.

PNI had the lowest while ANS had the highest predictive power and discrimination ability in terms of having the lowest Likelihood ratio (15.7 for ANS *vs*. 7.89 for albumin, 8.17 for NLR, and 6.32 for PNI), highest chi-square value (14.1 for ANS *vs*. 6.50 for albumin, 9.94 for NLR, and 4.38 for PNI), and highest c-index (0.651 for ANS *vs*. 0.568 for albumin, 0.639 for NLR, and 0.624 for PNI). As reflected by the lowest likelihood ratio, highest chi-square value, and highest c-index, ANS had the highest predictive power for OS and discrimination ability compared to PNI and individual albumin and NLR.

Severe (grade 3 or higher) adverse events (SAEs) associated with CCRT in our patient cohort are shown in Table IV. The most common SAEs were leukopenia (36.6%), mucositis (30.1%), and anemia (22.0%). Patients in the ANS 2 group were significantly associated with a higher incidence of infection (30.3%) than those in the ANS 0 (10.3%) and ANS 1 groups (9.8%).

Discussion

The role of systemic inflammation has been a topic of interest in several fields of oncology (11, 12). While several biomarkers have been widely used to reflect the nutritional and inflammatory status of cancer patients, their roles in different malignancy types and treatment settings have established different predictive or prognostic roles. The present prospective observational study demonstrated that an elevated ANS score, which is a nutritional and inflammation-based prognostic score, is associated with a lower surgical resection rate, greater CCRT incompletion rate, and shorter survival in patients with locally advanced esophageal cancer.

The relationship between inflammation and malignant tumors is tricky. It is postulated that tumors producing inflammatory cytokines are infiltrated by leukocytes (13-15); however, advanced neoplasms are associated with a defective systemic immune response. On the other hand, malnutrition has a direct relationship with malignancy. For example, in several studies, hypoalbuminemia is often used as a malnutrition and cachexia index, leading to a poor prognosis in various cancers (16, 17). Since both systemic inflammation and malnutrition contribute to worse survival outcomes in malignancy, high ANS, which incorporates elevation of NLR levels and hypoalbuminemia, is a possible independent prognostic indicator for worse prognosis (18). Taken together, the systemic nutritional and immunological status of patients may affect prognosis through local tumor immunity.

In recent literature, several indicators of nutritional and immunological statuses have been developed to evaluate the prognosis of gastrointestinal cancers (19-21). Amongst them, ANS and PNI both utilize albumin and differentiated white blood cells (WBC). The ANS categorizes patients according to the empirical level of albumin count and N/L ratio, classifying patients into three groups. However, while the PNI score is quantified through the addition of albumin count and lymphocyte count, a cutoff stratified patients into two groups. In the recent largest study of immunonutritional factors in esophageal cancer, Okadome *et al*. demonstrated that PNI has shown prominent prognostic significance in patients with curatively resected esophageal cancer (22). Our study revealed a significant correlation between ANS and PNI, while both utilized albumin and WBC counts. While the PNI only stratifies patients into two groups, the ANS is able to identify patients with the worst survival outcome among the three groups, thus providing more accurate prognostic information for patients and clinicians. In the role of NLR in esophageal cancer review by Pirozzolo *et al*., the benefit of accounting for neutrophil count by the ratio between neutrophil count and lymphocyte

Table IV. *Chemoradiotherapy-related grade III or higher adverse events.*

Adverse events	Entire cohort (n=123) n (%)	ANS 0 (n=39) n (%)	ANS 1 (n=51) n (%)	ANS 2 (n=33) n (%)	*p*-Value
Hematological toxicity					
Leukopenia	45 (36.6)	13 (33.3)	20 (39.2)	12 (36.4)	0.85
Anemia	27 (22.0)	5 (12.8)	11 (21.6)	11 (33.3)	0.11
Neutropenia	23 (18.7)	4 (10.3)	10 (19.6)	9 (27.3)	0.18
Thrombocytopenia	13 (10.6)	4 (10.3)	5 (9.8)	4 (12.1)	0.94
Neutropenic fever	8 (6.5)	2 (5.1)	3 (5.9)	3 (9.1)	0.77
Non-hematological toxicity					
Mucositis	37 (30.1)	10 (25.6)	12 (23.5)	15 (45.5)	0.041
Infection	19 (15.4)	4 (10.3)	5 (9.8)	10 (30.3)	0.022
Hyponatremia	17 (13.8)	4 (10.3)	8 (15.7)	5 (15.2)	0.74
Hypokalemia	11 (8.9)	2 (5.1)	6 (11.8)	3 (9.1)	0.55
Emesis	11 (8.9)	5 (12.8)	5 (9.8)	1 (3.0)	0.34
Hypertension	10 (8.1)	2 (5.1)	5 (9.8)	3 (9.1)	0.70
Hyperglycemia	7 (7.9)	2 (6.9)	1 (2.8)	4 (16.7)	0.14

*Indicates difference among three ANS patient groups.

count was addressed (23). As a ratio, different ranges between laboratories should have a limited impact on the presentation of the immunological status. It would also eliminate the heterogeneity in the cutoff definition or heterogeneity in patient populations (age, sex, geographical origin, and exposition).

Our multivariate analysis revealed that while the common prognostic factors of malignancy, including ECOG performance status and tumor length, are consistently valuable prognostic factors, the ANS is also an independent marker of poor prognosis in patients with locally advanced esophageal cancer. As the ANS also has the advantage of easy procurement prior to surgical intervention, it may be used as a part of routine evaluation during advanced esophageal cancer treatment planning.

While unaffected NLR and normal albumin level have independently shown better survival probability, a combination of the two factors, ANS, can stratify patients' survival more precisely. Notably, unaffected systemic nutritional and immunological status, that is, normal ANS, shows a distinct survival probability to an elevated ANS. As shown in our study, while elevated ANS showed a median survival of 11.4-13.8 months, the median survival of a normal ANS was not reached after 22 months of follow-up, indicating a pronounced difference. As our study enrolled patients with operable stage II-Iva esophageal cancer undergoing CCRT and sequential surgical resection with curative intent, we were able to evaluate the surgical resection rate. While treatment of locally advanced esophageal cancer involves a series of events, ANS was able to predict chemotherapy, radiotherapy, and surgical completion rates. At the beginning of chemoradiation, an ANS score of 2 indicated a significantly lower likelihood of completion of radiotherapy and chemotherapy. Progressing to surgical intervention, a normal ANS showed markedly greater complete surgical resection. Eventually, a normal ANS signifies a greater benefit from curative CCRT with sequential operation.

This is the first prospective study to assess the value of the ANS and its direct comparison with the PNI in patients with advanced esophageal cancer treated with CCRT. However, this study had certain limitations. For example, NLR and albumin were collected at a single time point, which may be influenced by transient conditions, such as infection or allergy. While our study did not distinguish between the reasons for abnormal NLR and albumin level, clinicians may need to be aware of acute conditions that may lead to ANS misinterpretation. Furthermore, our study used the median value of NLR and albumin as arbitrary cutoff points for ANS calculation. While they may be easily accessible, the most appropriate albumin and NLR cutoff values need further clinical validation for universal clinical application.

Conclusion

By incorporating the nutritional and inflammatory status of the patient, the pre-treatment ANS has survival prognostic specificity, which can identify esophageal cancer patients who are most likely to benefit from concurrent chemoradiotherapy. In this parallel setting, the ANS demonstrated better predictability than the PNI did. While exploration of inflammation markers on cancer prognosis has been a mainstream focus, our study supports future focus on the role of ANS in various malignancies for better clinical decision-making.

Conflicts of Interest

The Authors declare that no competing interests exist in relation to this study.

Authors' Contributions

Conception and design of study: HWH, HSW, YKY, HYS, CWC; Acquisition of data: HWH, HSW, HMM, LSY, TCK, HCY; Analysis and interpretation of data: HWH, HSW, CWC; Drafting of the manuscript: HWH, HSW, YKY, HYS, HMM, LSY, TCK, HCY, CWC.

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