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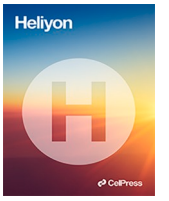

Positive lymph node ratio is an important index to predict long-term survival for advanced esophageal squamous carcinoma patients (II∼III) with R0 resection--a SEER-based analysis

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ABSTRACT

Background: Esophageal squamous carcinoma (ESCC) is one of the most malignant cancers in the world due to nodal metastasis. Therefore, a reasonable nodal staging system is extremely important for further treatment strategies. Recently the positive lymph node ratio (PLNR) is an important prognostic factor in various solid tumors

Method: In this study, we investigated the clinical significance of the PLNR in stage II∼III ESCC patients. We collected the pathological characteristics of 272 stage II∼III ESCC patients from the SEER database from 2004–2016. ROC curves were used to calculate the best cutoff value of the PLNR; Pearson's Chi-square ($\chi 2$) and Fisher's exact probability tests were used to compare the clinical baseline and characteristics of patients. For continuous variables, Student's *t*-test and ANOVA were performed to evaluate statistical significance. Clinical outcomes were estimated by using the Kaplan−Meier method and log-rank test. Furthermore, univariate and multivariate Cox regression models were utilized to analyze independent prognostic factors of ESCC patients.

Results: Consequently, advanced ESCC patients were effectively stratified into two groups by prognosis using a PLNR cutoff value of 0.15 (P value = 0.04). The median survival time of patients with PLNR <0.15 (n = 145) was much higher than that of patients (n = 127) in the PLNR ≥0.15 group (20.0 vs. 13.0 months, P value < 0.0001). Notably, the PLNR significantly predicted the prognosis of ESCC patients with stage N1 (P value 0.01) and stage III (P value < 0.001) disease. The multivariate Cox proportional hazard model showed that T stage (HR 1.33, 95 % CI 0.97–1.82), tumor size >45 mm (HR 1.32, 95 % CI 1.02–1.70), N stage (HR 1.41, 95 % CI 0.98–2.01) and PLNR ≥0.15 (HR 1.35, 95 % CI 0.87–1.74) were independent risk factors for prognostic prediction in ESCC patients. Meanwhile, 117 II∼III ESCC patients from Shaanxi Provincial People's Hospital shown that the overall survival with a PLNR <0.15 (n = 96) was significantly longer than that with a PLNR ≥0.15 (n = 21) .

Conclusions: The PLNR is useful for accurately predicting clinical outcomes and determining postoperative strategies.

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1. Introduction

Esophageal cancer ranks as the seventh most common cancer and the sixth leading cause of cancer-related death worldwide [1]. Meanwhile, the incidence of esophageal cancer is still rapidly rising worldwide, especially in Asia [2–4]. Among esophageal carcinomas, squamous cell carcinoma is the main pathological type, with an approximately 10~15 % 5-year survival rate despite multiple treatment approaches [3–5]. The reason for the particularly poor prognosis in esophageal squamous cell carcinoma (ESCC) is extensive lymph node metastasis [5]. Currently, radical esophagectomy is considered the first curative choice for advanced ESCC patients (II~III). Two pivotal factors determine postoperative prognosis of esophageal carcinoma—the range of primary lesion and lymphatic metastasis. However, are other important indicators ignored in clinical practice? For example, do the N1 stage patients with 1 metastasis to 1 lymph node and 10 examined lymph nodes have same postoperative prognosis as patients with metastasis to 1 lymph node and 20 examined lymph nodes? Therefore, appropriate surgical treatment for lymph node dissection and the lymph node staging system should be considered again.

The positive lymph node ratio (PLNR) is defined as the total pathological metastatic lymph node number/total retrieved lymph node number [6–12]. It has been reported as a promising index to predict prognosis in different cancers. In gastric cancer, a PLNR of 0.4 was regarded as the best cutoff value to stratify long-term survival in pN3 patients [7]. Other evidence suggested that the lymph node ratio (LNR) was superior to pN stage (UICC/AJCC) as an independent factor for prognostic prediction in remnant gastric cancer with insufficient lymph node resection (<15 nodes) [12]. In lung cancer, although postoperative radiation therapy (PORT) cannot

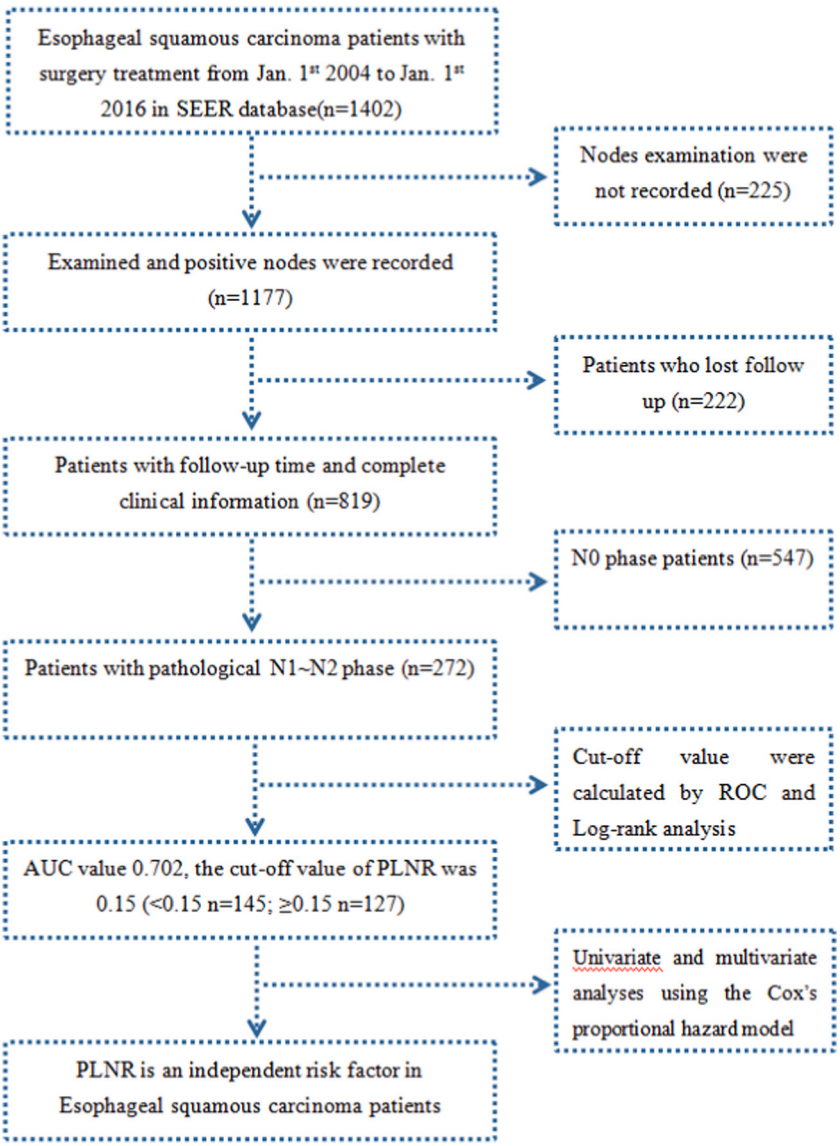

Fig. 1. Flowchart of screening eligible advanced ESCC patients.

improve overall survival for all patients with pN2 non-small cell lung cancer, patients with a PLNR>0.31 might benefit from PORT regardless of chemotherapy status [10]. Moreover, a sentinel lymph node ratio >0.333 showed the highest diagnostic efficiency, with an area under the ROC curve (AUC) of 0.726 in breast cancer [9]. The significance of the PLNR has also been reported in adenocarcinoma of the esophagogastric junction (AEG) [6]. The PLNR cutoff value > 0.1 was significantly correlated with tumor diameter>4 cm, tumor depth, greater pathological N-status and pathological stage. However, only a few studies have been focused on the relationship between the PLNR and long-term survival in esophageal cancer patients. Therefore, the importance of the PLNR should be further explored in advanced ESCC patients.

Because of insufficient clinical trial data, we collected the clinicopathological characteristics of ESCC patients from the Surveillance, Epidemiology, and End Results (SEER) database and retrospectively analyzed the relationship between the PLNR and long-term survival outcomes of II∼III ESCC patients. Our results could be used to develop selection criteria for the application of lymph node resection and provide more information for postoperative treatment in advanced esophageal cancer patients.

2. Method

2.1. Data source

Using the National Cancer Institute SEER*Stat software version 8.3.6 (seer.cancer.gov/seerstat), we retrieved the clinical data of 1402 patients diagnosed with primary esophageal squamous carcinoma from January 1, 2004, to January 1, 2016. The SEER database is derived from 18 cancer registries representing approximately 28 % of patients in the United States [13]. Among them, 225 patients without lymph node resection information were excluded. Then, 222 patients who were lost to follow-up were also excluded. From 819 patients, we screened 272 patients with N1∼N2 stage disease after surgical treatment (Surgery Code A300, A400, A500∼A550). In this study, none of the patients underwent preoperative chemo- or chemoradiotherapy. Clinical characteristics, including age at diagnosis, sex, tumor size, T stage, N stage, nuclear grade, positive lymph node number, examined lymph node number, PLNR, marital status, and survival time, were further analyzed. Overall survival (OS) was considered the main point of this study. Meanwhile, eligible patients were identified under the same conditions. Finally, we used the AJCC/UICC TNM classification system [14] to evaluate the compatibility of our findings in ESCC. The whole flowchart is shown in Fig. 1. Then, we retrospectively collected the clinical information of 117 advanced ESCC patients from the thoracic department of Shaanxi provincial people's hospital from January 1, 2013, to June 30, 2022. The last follow-up was 2023 Jun 30th. Age at diagnosis, sex, tumor size, tumor location, surgical approaches, T stages, N stages, nuclear grades, positive lymph node numbers, examined lymph node numbers, marital status, and survival time were included in this research.

2.2. Study procedures

To evaluate the clinical importance of the PLNR in advanced esophageal squamous cancer, we first calculated the PLNR by the following formula: PLNR = total pathological metastatic lymph node numbers/total retrieved lymph node numbers. We explored the PLNR cutoff value by using ROC curves. In addition, we examined the ability to stratify the prognosis in each cutoff value of the PLNR. Second, we compared the related clinicopathological factors between patients with different PLNRs. Finally, univariate and multivariate analyses using Cox's proportional hazard model in N1∼N2 ESCC patients were performed to detect whether the best cutoff value was an independent risk factor for clinical outcome.

2.3. Statistical analysis

The best cutoff value of the PLNR was calculated by using the ROC curve; Pearson's Chi-square ($\chi 2$) and Fisher's exact probability tests were used to compare the clinical baseline and characteristics of patients between different groups. Continuous variables, such as age, tumor size, and examined and positive lymph nodes, are expressed as the mean ± standard deviation. Student's *t*-test and *ANOVA* were performed to evaluate the statistical significance of continuous variables. Clinical outcomes were estimated by using the Kaplan–Meier method, and the log-rank test was used to examine significant differences. Furthermore, univariate and multivariate Cox regression models were utilized to analyze independent prognostic factors for the overall survival of ESCC patients. A P value < 0.05 was considered a significant difference. Statistical analyses were performed with SPSS software (version 24.0; IBM, Chicago, IL) and GraphPad Prism software (Version 6.01).

3. Result

3.1. Basic clinicopathological characteristics of ESCC patients

A total of 272 advanced ESCC patients (II∼III) were enrolled in this study, including 187 males (68.7 %) and 85 females (31.7 %). Patients more than 65 years old accounted for 47.4 % (n = 129), and those less than 65 years old accounted for 52.5 % (n = 143). Among these, there were 212 N1 patients (77.9 %) and 60 N2 patients (22.1 %). The study group consisted of stage IIB 26, stage IIIA 37 and stage IIIB 209 patients. The mean number of examined lymph nodes was 18.1 (range of 1∼80), and the mean number of positive lymph nodes was 1.94 (range of 1∼6). The average tumor size in ESCC patients was 45.1 mm (1–135 mm). Furthermore, there were 11 G1 (4 %), 130 G2 (47.8 %) and 131 G3 (48.2 %) patients.

3.2. Cutoff value of the PLNR to stratify prognosis

As shown in Fig. 2A, through data analysis and ROC curve construction, the best cutoff value of the PLNR was 0.15. Generally, the cohort of 272 patients was divided into the PLNR<0.15 group (145 patients) and the PLNR ≥0.15 group (127 patients). The criterion showed the highest diagnostic efficiency for the long-term survival of ESCC patients, with an area under the ROC curve of 0.702 (P value 0.04). The specificity of the ROC curve was 78.3 %, and the sensitivity was 50.3 %. Furthermore, we performed survival analysis using different cutoff values, such as 0.1, 0.15, 0.20, 0.25, 0.30, and 0.4, to verify our findings (Fig. 2B). Consistent with our previous conclusion, a cutoff value of 0.15 was most effective for stratifying the prognosis of advanced ESCC patients (P value 7.0×10^{-6}, 3-year survival rate: PLNR<0.15 vs. PLNR ≥0.15 29.1 % vs. 11.6 %; Table 1) as presented in Fig. 2C. The median survival time of patients with a PLNR <0.15 (n = 145) was 20.0 months, and that of patients with a PLNR ≥0.15 (n = 127) was 13.0 months (P value < 0.0001).

3.3. Subgroup analysis of the prognostic efficiency of the PLNR

In the subgroup analysis, a cutoff value of 0.15 was a significant index to predict clinical outcomes in N1 stage patients (presented in Fig. 3A). Between different groups, the long-term survival of ESCC patients (n = 137) with a PLNR<0.15 was markedly higher than that of patients (n = 75) with a PLNR ≥0.15 (median survival time 20.0 vs. 16.0 months; P value = 0.01). Interestingly, we did not observe significant differences in N2 patients (6 vs. 9.5 months P value = 0.67; Fig. 3B). Moreover, 37 stage IIIA and 209 stage IIIB ESCC patients were assigned to two groups according to the PLNR cutoff value. Notably, there was a significant difference between the different groups in stage IIIA and IIIB patients (Fig. 4). The PLNR was negatively associated with the long-term survival of ESCC patients. The median survival time of stage IIIA patients with a PLNR<0.15 (n = 24) was 27.5 months, which was much higher than that of patients (n = 13) in the other group (10.0 months P value < 0.001, as shown in Fig. 4A). For stage IIIB ESCC patients (Fig. 4B), the data suggested that the PLNR<0.15 patients (n = 103) had 17.0 months and the PLNR ≥0.15 group was only 12.0 months (n = 106), exhibiting a significant difference between the two groups (P value < 0.001).

3.4. Comparison of clinicopathological factors between patients with a PLNR <0.15 and a PLNR ≥0.15

Subsequently, we compared clinicopathological characteristics between the two groups. As shown in Table 2, compared with PLNR

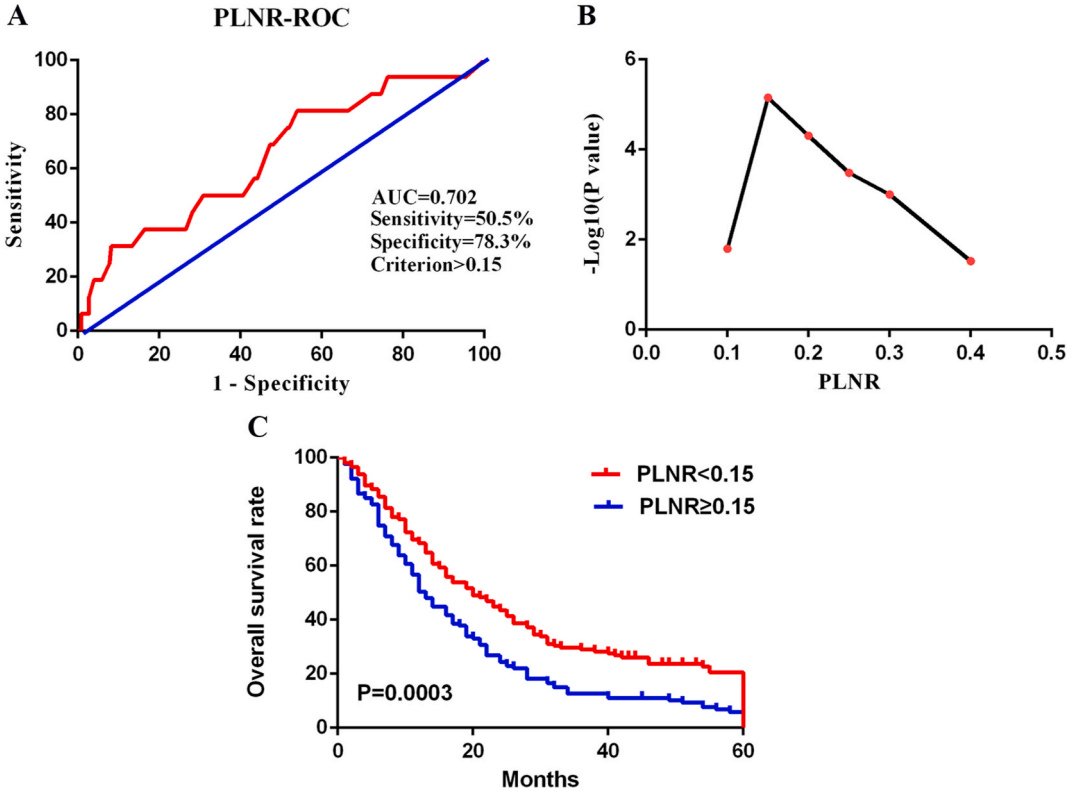

Fig. 2. (A) ROC curve to evaluate the diagnostic efficiency of the PLNR for advanced ESCC patients, AUC 0.702 and P value 0.04; (B) different cutoff values of the PLNR were examined again, and 0.15 could most significantly stratify the prognosis of ESCC patients (detailed data presented in Table 1); (C) The survival curve of PLNR <0.15 (n = 145) and PLNR ≥0.15 patients (n = 127) using the Kaplan–Meier method (the median survival time of the two groups was 20.0 vs. 13.0 months, P value < 0.0001).

Table 1
The ability of different cut-off values to stratify prognosis of advanced ESCC patients into two groups (P-value 7.0×10^{-6}; 3-year survival rate: 29.1 % vs 11.6 %); The -Log (P-value) was plotted as line-chart and shown in Fig. 2B.

			Survival rate (%)			
Cut-off	Value	n	1yrs	3yrs	5yrs	*P*-Value
0.1	<0.1	110	71.8	26.4	18.7	0.016
	≥0.1	162	58.0	17.8	1.7	
0.15	<0.15	145	69.5	29.1	1.1	7.0×10^{-6}
	≥0.15	127	47.9	11.6	1.0	
0.2	<0.2	176	69.3	26.1	1.4	4.9×10^{-5}
	≥0.2	96	42.7	12.5	0.8	
0.25	<0.25	199	67.3	24.1	1.7	3.3×10^{-4}
	≥0.25	73	39.7	13.7	0.7	
0.3	<0.3	211	65.4	23.7	1.6	0.001
	≥0.3	61	41.0	13.1	0.7	
0.4	<0.4	236	63.1	22.4	2.8	0.03
	≥0.4	36	38.9	13.9	0.6	

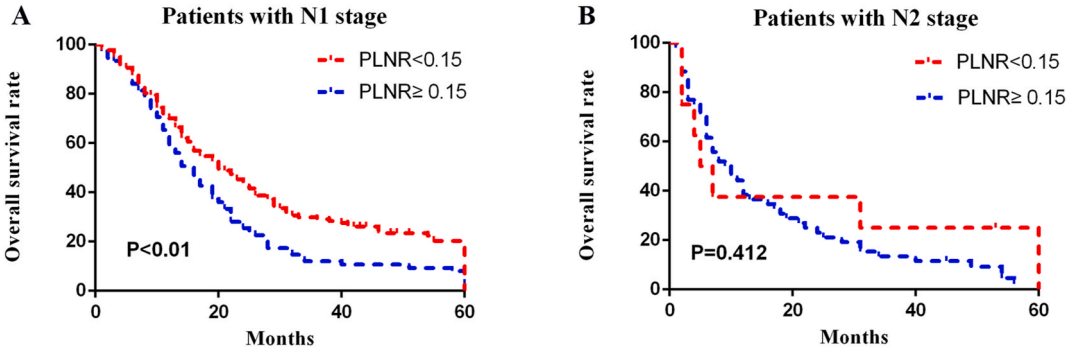

Fig. 3. The Kaplan–Meier method and log-rank test were performed to study long-term survival between PLNR <0.15 and PLNR ≥0.15 patients according to N stage. (A) The median survival of PLNR <0.15 (n = 137) vs. PLNR ≥0.15 (n = 75) patients with N1 stage 20.0 vs. 16.0 months; P value = 0.01; (B) Survival time in N2 stage, the number of patients in PLNR <0.15 and ≥ 0.15 were 8 and 52 (6 vs. 9.5 months P value = 0.67).

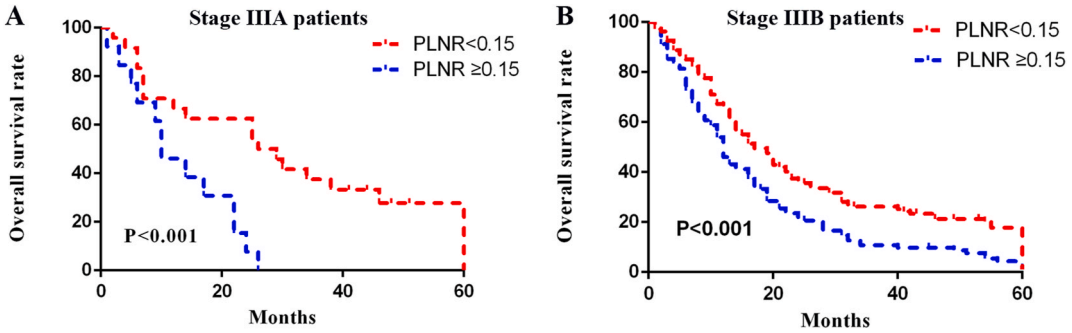

Fig. 4. The clinical outcomes of different PLNR patients were explored by using the Kaplan–Meier method and log-rank test in stage IIIA and IIIB. (A) The clinical prognosis for PLNR <0.15 patients (n = 24) was much better than that for patients (n = 13) in PLNR ≥0.15 (27.5 vs. 10.0 months; P value < 0.001); (B) The results demonstrated that the median survival time of stage IIIB patients with PLNR <0.15 (n = 103) was 17.0 months, which was markedly higher than that of PLNR ≥0.15 patients (n = 106, 12 months, P value < 0.001).

≥0.15 patients, significant differences were observed only in positive lymph nodes (P < 0.001) and examined nodes (P < 0.001). Those in the PLNR <0.15 group had fewer positive lymph nodes (1.4 vs. 2.6) and more examined lymph nodes (19.9 vs. 8.9). Surprisingly, the results for G stage, T stage and tumor size did not present meaningful differences between the PLNR <0.15 and ≥ 0.15 groups.

Univariate and multivariate analysis using the Cox proportional hazard model for different PLNR patients.

Verifying prognostic factors, univariate and multivariate analyses using Cox's proportional hazard model illustrated that T stage (P value 0.031, HR 1.33, 95 % CI 0.97–1.82), tumor size >45 mm (P value 0.033, HR 1.32, 95 % CI 1.02–1.70), N stage (P value 0.001, HR 1.41, 95 % CI 0.98–2.01) and PLNR ≥0.15 (P value 0.0001, HR 1.35, 95 % CI 0.87–1.74) were independent poor prognosis factors in stage II~III ESCC patients. The results are shown in Table 3.

Table 2
Comparison of clinical characteristics between two groups according to PLNR cut-off value.

		PLNR			
Subjects,n	Total,n	<0.15 (n = 145)	≥0.15 (n = 127)	χ2	P-value
Age					
<65	143	84	59	3.575	0.059
≥65	129	61	68		
Sex					
Female	85	47	38	0.196	0.658
Male	187	98	89		
Grade					
G1	11	5	6	0.469	0.791
G2	130	68	62		
G3	131	72	59		
Pathological T stage					
T1+T2	66	40	26	1.365	0.172
T3+T4	206	105	101		
Pathological N stage				49.424	**<0.0001**
N1	212	137	75		
N2	60	8	52		
Stages					
II	31	19	12	1.028	0.311
III	244	126	118		
Tumor size (mm)	Median (range)	45.6 (7–120)	44.5 (11–129)	–	0.699#
Positive node	Median (range)	1.4 (1–6)	2.6 (1–6)	–	**<0.0001#**
Examined node	Median (range)	19.9 (7–80)	8.9 (1–37)	–	**<0.0001#**

#Student's *t*-test; Other characteristics were evaluated by using chi-square (χ2) test.

Table 3
Univariate and multivariate analyses using the Cox's proportional hazard model in ESCC patients.

Variables		n	Univariates[a]	Multivariate	analysis[b]	
			P-value	HR	(95 % CI)	P-value
Age	<65 vs ≥ 65	143 *vs* 129	**-**	**-**	**-**	**-**
Sex	Female vs Male	85 *vs* 187	–	–	–	–
T stage	T1+2 vs T3+4	62 *vs* 210	**0.006**	**1.33**	**0.97–1.82**	**0.031**
Tumor size (mm)	<45 vs ≥ 45	149 *vs* 123	**0.01**	**1.32**	**1.02–1.70**	**0.033**
G	G1+2/G3	141 *vs* 131	–	–	–	–
N stage	N1 vs N2	212 *vs* 60	**0.0001**	**1.41**	**0.98–2.01**	**0.001**
PLNR	<0.15 vs ≥ 0.15	145 *vs* 127	**0.0003**	**1.35**	**0.87–1.74**	**0.0001**

HR hazard ratio, CI confidence interval.
a:Log-rank test.
b:Multivariate survival analysis was performed using the Cox's proportional hazard model.

3.5. Prognostic efficiency was evaluated by our own data

The basic clinicopathological characteristics of 117 II~III patients are presented in Supplemental Table 1. We also categorized those 117 patients into two groups according to the PLNR. The prognostic efficiency of the PLNR was proven again by our own data. As shown in Supplemental Fig. 1, the overall survival of ESCC patients with a PLNR <0.15 (n = 96) was significantly longer than that of patients with a PLNR ≥0.15 (n = 21) (median survival time: 34.0 months vs. 22.0 months; P = 0.04). In stage III patients (Supplemental Fig. 2A), the long-term survival of ESCC patients (n = 93) with a PLNR <0.15 was 31.0 months, and that of patients with a PLNR ≥0.15 (n = 20) was only 25.0 months. A significant difference was observed between the two groups (P = 0.04). The number of stage II patients was too limited (n = 4). Interestingly, the data of pN2 patients did not show a marked difference, which was consistent with our previous results (Supplemental Fig. 2B).

4. Discussion

Esophageal squamous carcinoma is one of the most common cancers in the world and has caused an enormous burden on human health. In addition, the occurrence of ESCC in China is extremely frequent, such as in the Taihang area, Heinan and Heibei provinces [2–4]. Although clinical doctors have constantly developed new technologies and methods, such as video-assisted thoracic surgery (VATS), neoadjuvant chemoradiotherapy, immunotherapy or targeted therapy, to improve the outcomes of ESCC patients, the

long-term survival of ESCC patients is still poor at 10–30 % because of lymph node metastasis and primary recurrence [2–5]. Currently, the treatment of patients with esophageal cancer is based on the TNM staging system. However, in clinical practice, we noticed that patients with more positive lymph nodes or fewer examined lymph nodes seem to show poor survival outcomes among same-stage patients. Therefore, it is important to reassess prognostic factors by using a more accurate index.

In this study, we performed the PLNR to predict the prognosis of advanced ESCC patients based on SEER data, which had been analyzed in only a few studies of esophageal squamous carcinoma. Our results showed that PLNR = 0.15 was the best cutoff value to stratify the clinical outcomes of ESCC patients (P value 0.04). The area under the ROC curve was 0.702 (between effective value 0.70–0.90). Another method to evaluate the best cutoff value of the PLNR also showed that 0.15 was meaningful (-Log P value = 5.15) for advanced ESCC patients (Fig. 1B). Strikingly, the survival curve demonstrated that PLNR <0.15 patients had much better long-term survival than those in another group (20.0 vs. 13.0 months P value < 0.0001). Interestingly, a significant difference could be observed in ESCC patients with N1 stage (P value 0.01) rather than N2 stage (P value 0.67). The reason for this phenomenon might be fewer patients in the N2 group (n = 60). However, the results showed that the two survival lines of the N2 group separated after 20 months, which suggested that the PLNR might be a potential prognostic factor for long-term survival in N2 patients. The reason for excluding pN0 patients is that the lymph node ratio of N0 patients is 0 %, and it is meaningless to evaluate the significance of the PLNR in N0 patients. In addition, the number of cases of pN3 patients were limited (n = 20), and it was too difficult to make a precise conclusion based on such a small sample. Meanwhile, most pN3 patients were classified as stage IVA and accepted chemo-or chemoradiotherapy. Therefore, those patients were excluded from this study. Meanwhile, the PLNR showed a better prognostic prediction for stage III ESCC patients. There were few ESCC patients with stage II disease (n = 26), and we could not analyze the accuracy of the PLNR in those patients. After multivariate Cox analysis, T stage, N stage, tumor size and PLNR were independent factors of patient prognosis with advanced ESCC. G was not meaningful in advanced patients, which was consistent with the NCCN guidelines in the tumor staging system. In this research, the PLNR system could reflect various clinical factors: the extent of lymphadenectomy and the differences in innate lymph nodes among individuals and the surgical level of surgeons. Even in the same stages or N, insufficient retrieved lymph nodes may be closely related to poor clinical outcomes and further treatment decisions. Therefore, our results suggested that an eligible and radical esophagectomy must be based on sufficient lymph node resection. NCCN guidelines recommend that the number of examined lymph nodes should be more than 15. While elderly ESCC patients (>60 years old) have poor physical and psychological conditions, extensive lymph node resection might increase surgical trauma and postoperative complications, such as anastomotic leakage, recurrent laryngeal nerve injury, and pneumonia. Therefore, we are investigating a study to determine reasonable lymphadenectomy in elderly ESCC patients using artificial intelligence (this study is not complete, and the results will be shown in the future). Furthermore, the PLNR could be considered a new index for postoperative treatment. ESCC patients with a PLNR ≥0.15 might accept postoperative adjuvant therapy after R0 resection.

Our own data from Shaanxi Provincial People's Hospital were used to verify previous results. As shown in Supplemental Fig. 1, the long-term survival of ESCC patients with a PLNR <0.15 was much better than that of patients with a PLNR ≥0.15, which was consistent with the results in stage III and N2 patients. The cases of stage II (n = 3) and N1 with PLNR <0.15 (n = 1) patients were too limited; therefore, we did not use the log-rank test to examine significant differences between the two groups. Meanwhile, the number of examined lymph nodes in our data was much higher than that in the data from SEER (29.2 vs. 14.7), which might suggest that Chinese thoracic surgeons were good at surgical techniques.

The PLNR as a prognostic index has been reported in various malignancies, such as gastric cancer, esophagogastric junction adenocarcinoma (AEG) [6], colorectal cancer [15,16] and non-small cell lung cancer [10,11]. Namely, various cutoff values of the PLNR for the new nodal staging system have been recommended. Zhang et al. reported that patients with a PLNR >0.4 had a shorter 5- and 10-year disease-specific survival (DSS) rate (8.5 %, 1.4 %) than those with a low PLNR (58.0 %, 27.5 %) in Siewert type II AEG after a 10-year follow-up [17]. Our conclusion was proven by Hao-Xian Yang et al. [18]. They divided the PLNR into four groups: PLNR = 0, PLNR 0∼0.1, PLNR 0.1–0.3 and PLNR >0.3 and suggested that the survival rate of ESCC could be discriminated between the four groups and that the PLNR was meaningful to compensate for the insufficiency of nodal staging. The role of postoperative radiation therapy (PORT) for patients with pN2 non-small cell lung cancer was determined by the sampled lymph node ratio. Nikhil P. suggested [11] that patients with a PLNR >0.5 might benefit from PORT. Other researchers revealed that PORT appeared to be an optimal strategy for T2, grade I∼II and LNR >0.31 in non-small cell lung cancer patients [10]. Furthermore, less lymph node yield (<12) was associated with poor disease-free survival (DFS) and overall survival (OS) in stage III colonic cancer [19]. There was also increasing evidence to prove that the positive lymph node ratio could stratify prognosis in gastric cancer [7,8,12]. The best cutoff value in pN3 gastric cancer patients was 0.4, and the lymph node ratio was an independent prognostic indicator in remnant gastric cancer [20]. However, Masatoshi et al. suggested that lymph node ratio (c-index 0.701 95% CI: 0.627-0.775) was not better than pN stage (7th UICC c-index 0.700 95 % CI: 0.627–0.771) [21]. Consistent with our findings, Wenzhu Yao demonstrated [22] that a positive lymph node ratio (LNR) > 0.16 was an independent risk factor affecting the prognosis of esophageal cancer patients (LNR <0.16 vs. LNR≥0.16: HR = 1.827, 95 % CI: 1.140–2.929; P = 0.000). Moreover, the PLNR was used to determine postoperative treatment in ESCC patients [23]. The patients in the group with a higher LNR who had undergone adjuvant therapy showed a significantly better survival than those without adjuvant therapy (P value 0.030).

Although we explored whether the PLNR (best cutoff value: 0.15) was highly associated with prognosis in ESCC patients, some drawbacks in this research could not be ignored. First, different levels of enthusiasm and habits for optimal lymphadenectomy between Western and Eastern countries might exist. The data from SEER did not entirely reflect the clinical characteristics of Chinese ESCC patients. Therefore, we retrospectively collected ESCC samples (n = 412) from the thoracic department of Shaanxi Provincial People's Hospital, and we planned to analyze the long-term survival of those patients from the real world in future studies. Second, the constituent ratio of ESCC patients was not very reasonable in this study; 77.9 % of patients (n = 212) had stage N1 disease. Therefore, we

did not observe a significant difference in ESCC patients with N2 stage disease. In addition, it was necessary to resect more than 15 lymph nodes for appropriate N staging using the 8th TNM classifications. Some patients from the SEER database had only a small number of retrieved lymph nodes, which was negatively related to clinical outcomes. Finally, other important factors, such as mutation types, PD-1/PD-L1 status, Ki-67 rate and postoperative treatment, were not collected in the SEER database, which made further investigation difficult. With our study, we created a new perspective for thoracic surgeons to evaluate prognosis and postoperative treatment in ESCC patients.

5. Conclusion

In conclusion, the PLNR is an independent index for prognostic prediction in ESCC patients. The best cutoff value of the PLNR was 0.15. We can evaluate the prognosis of advanced ESCC patients (II∼III) and detect more malignant cases for further treatment precisely using the new nodal staging system.

Ethics approval

This study was a retrospectively analysis using public database and data from Shaanxi Provincial People's Hospital without ethics approval.

Consent for publication

Not applicable.

Availability of data and materials

The data that support the findings of this study are available from the corresponding author upon reasonable request and SEER public database.

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Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request and SEER public database. The raw data of SEER database and our own department were uploaded into website.

CRediT authorship contribution statement

Bin Hou: Writing – review & editing, Writing – original draft, Software, Methodology, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Jinyan Yuan:** Resources, Investigation, Data curation. **Shuge Kang:** Resources, Investigation, Data curation. **Yuanye Yang:** Resources, Investigation, Data curation. **Xing Huang:** Resources, Investigation, Data curation. **Hui Xu:** Resources, Investigation, Data curation. **Kai Guo:** Supervision, Funding acquisition, Conceptualization. **Wei Tian:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Conceptualization.

Declaration of competing interest

All authors declared no potential conflicts of interest with respect to the research, author-ship, and/or publication of this article.

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Not applicable.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2023.e22600.

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