Clinical application value of the prognostic nutritional index for predicting survival in patients with oesophageal squamous cell carcinoma undergoing chemoradiotherapy or radiotherapy

Ling Xiao
Sichuan Cancer Hospital and Research Institute https://orcid.org/0000-0003-2291-9459
Jiahua Lyu
Sichuan Cancer Hospital and Research Institute
Xiao Liu
Sichuan Cancer Hospital and Research Institute
Ke Li
Sichuan Cancer Hospital and Research Institute
Yuan Wang
Sichuan Cancer Hospital and Research Institute
Rongke Zhang
Sichuan Cancer Hospital and Research Institute
Taiyu Chen
Sichuan Cancer Hospital and Research Institute
Tao Li (lttgzy@163.com)
Sichuan Cancer Hospital and Research Institute

Research

Keywords: Oesophageal squamous cell carcinoma, chemoradiotherapy, prognostic nutritional index, prognosis

Posted Date: March 4th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-16066/v1

Abstract

Background : The prognostic nutrition index (PNI) has been shown to have prognostic value for several common cancers. The study aim was to explore the clinical application value of the PNI for prognosis of patients with oesophageal squamous cell carcinoma (ESCC) treated with radical chemoradiotherapy (CRT) or radiotherapy (RT).

Methods : Overall, 193 patients with ESCC who received radiotherapy with or without chemotherapy at Sichuan Cancer Hospital from March 20, 2012 to December 25, 2017 were retrospectively analysed. Based on serum measurements before treatment, the PNI at ESCC recurrence was calculated as albumin (g/L) + 5 × total lymphocyte count. The Kaplan–Meier method and Cox proportional regression model were used to analyse the relationship between PNI and overall survival (OS).

Results : The average pretreatment PNI of 193 ESCC patients was 49.01 ± 4.68. The optimal cutoff value of PNI was 47.975, and the patients were divided into a low-PNI group (<47.975) and a high-PNI group (≥47.975). PNI was related to tumour length, T-stage and synchronous chemotherapy in ESCC patients ($P < 0.05$). The median OS for the entire group was 22.37 months. The median OS of patients in the high-PNI group and low-PNI group were 32.63 months and 15.4 months, respectively, the 3-year survival rates were 47.5% and 32.2% and the 5-year survival rates were 37.7% and 16.8%, respectively, (all $P = 0.001$). Univariate analysis showed that PNI, tumour length, T-stage and synchronous chemotherapy were related to the prognosis of ESCC patients ($P < 0.05$). Multivariate analysis showed that tumour length ($P = 0.019$), synchronous chemotherapy ($P = 0.009$) and PNI ($P = 0.003$) were independent prognostic factors affecting the prognosis of patients in ESCC treated with RT or CRT.

Conclusions: The calculation of PNI value is simple, reliable and repeatable and can improve the accuracy of a patient's prognosis. Confirmation of these results by a large-sample prospective study is desirable.

Introduction

In recent years, oesophageal carcinoma has remained as one of the leading causes of morbidity and mortality of neoplastic diseases worldwide [1]. Adenocarcinoma is the predominant oesophageal cancer in the United States and Western countries. However, oesophageal cancer is predominantly squamous cell carcinoma in Asian countries, accounting for > 90% of cases in China [2]. Although progress has been made in surgery, chemoradiation and targeted therapy, the prognosis of oesophageal squamous cell carcinoma (ESCC) patients remains poor because of early recurrence or distant metastases, and many factors affect the prognosis, such as age, smoking history, drinking history, eating habits, clinical stage and treatment [3–5]. Studies have reported that 60–85% of oesophageal cancer patients have varying degrees of malnutrition, which is first among all tumours [6]. More and more studies have shown that the long-term prognosis of patients with malignant tumours is closely related to their nutritional status and immunity [7]. The prognostic nutrition index (PNI) was first used mainly to assess the nutritional status

before surgery, risk of surgery and postoperative complications [8]. Recent studies have shown that the PNI can be used as a new indicator to evaluate the prognosis of various malignant tumours, such as liver cancer, colorectal cancer, pancreatic cancer and gastric cancer [9–12]. However, to our knowledge, the prognostic value of pretreatment PNI values in ESCC patients treated with radical radiotherapy (RT) has not been studied. Therefore, the study aim was to explore the clinical value of PNI for the prognosis of patients with ESCC who had undergone radical chemoradiotherapy (CRT) or RT.

Materials And Methods

Patients

This study was conducted according to the principles of the Declaration of Helsinki and its amendments and was approved by the ethics committee of the Sichuan Provincial Cancer Hospital. From March 20, 2012 to December 25, 2017, a retrospective analysis of 193 patients with radical CRT or RT for ESCC was performed. All of the patients included in the analysis met the following inclusion criteria: (I) diagnosis of ESCC but refused or could not tolerate surgery; (II) histologically or cytologically confirmed ESCC; (III) karnofsky performance status ≥ 70 points; (IV) treatment with an intensity-modulated radiation therapy dose ≥ 50 Gy (in 25–35 fractions over a range of 5–7 weeks) with 0 to 6 courses of concurrent chemotherapy; (V) data available from blood biochemical examination 1 week prior to treatment; (VI) no distant tumour metastasis; (VII) restaged according to the TNM classification system issued by the American Joint Committee on Cancer (AJCC; 7th edition, 2012).

Treatment

All patients underwent radical radiotherapy with or without chemotherapy. Total radiotherapy dose: 50 to 72.6 Gy, total radiotherapy frequency: 20 to 34 f. The primary tumour and any positive regional lymph nodes were defined as the gross tumour volume (GTV). Positive lymph nodes were determined by physical examination, endoscopy, cervical-thoraco-abdominal computed tomography (CT) or positron emission tomography-CT. A radial edge of 0.5 to 1.0 cm was provided around the GTV, and an edge of 3 cm in the proximal and distal directions was defined as the clinical target volume (CTV). The tumour movement was 0.5 cm of the CTV expansion to define the planned target volume. Patients receiving concurrent chemotherapy mainly received platinum single or combined chemotherapy, whereas elderly patients received oral chemotherapy or methotrexate for 1 to 6 cycles.

Calculation of PNI

The total number of lymphocytes in blood cell analysis and serum albumin levels in liver function were collected 1 week before treatment, during treatment (with the lowest detection value), and after treatment, PNI = serum albumin level (g/L) + 5 × absolute lymphocyte count.

Follow-up

At our institution, all patients were followed up through outpatient examinations and telephone calls. The last follow-up time was January 15, 2020. Survival time was measured from the first day of pathological diagnosis to death or last follow-up. The median follow-up time was 21.6 months (range: 2–91 months).

Statistical analysis

All recorded data were analysed by using SPSS version 25.0 (IBM Corporation, Armonk, NY, USA) and GraphPad Prism version 8.0.2 (GraphPad Prism Software, San Diego, California, USA). The t-test or analysis of variance was used to compare the continuous variables that fit the normal distribution. The χ^2 test was used to compare the counted data. The Kaplan–Meier method was used to calculate the OS rate. The Cox proportional hazards model was used for univariate and multivariate analysis to study the effect of different factors on survival. Covariates included age (< 65 years vs. ≥65 years), sex, smoking history, drinking history, karnofsky performance status (KPS) score (70 vs. 80 vs. 90), tumour location, tumour length (< 5 cm vs. ≥5 cm), clinical T-stage, clinical N-stage, TNM stage, body mass index (BMI), RT dose (< 60 Gy vs. ≥60 Gy), synchronous chemotherapy and PNI (< 47.975 vs. ≥47.975). P values < 0.05 were considered to be indicative of statistical significance. A receiver operating characteristic (ROC) curve for prediction was plotted to verify the optimal cutoff value for PNI.

Results

Patient and tumour characteristics

A total of 193 patients who met the enrolment criteria were included in this study, and their characteristics are presented in Table 1. Among the 193 patients, 149 (77.20%) were male and 44 (22.80%) were female. The median age was 64 years (range, 34–86 years). There were 110 patients (57%) with a smoking history and 83 patients (43%) without a smoking history. There were 110 patients (57%) with a drinking history and 83 patients (43%) without. Regarding the RT dose, 12 patients (6.22%) received <60 Gy and 181 (93.78%) received ≥60 Gy. Synchronous chemotherapy was administered in addition to RT to 170 (87.56%) patients, and 23 patients (11.92%) did not receive chemotherapy (Table 1).

Assessment of the PNI cutoff values

The optimal PNI cutoff values were analysed by ROC curves according to the overall survival (OS) of patients with ESCC. According to the ROC curve and Youden index, the ideal pretreatment PNI cutoff value was 47.975. The area under the ROC curve for the PNI was 0.605 (95% CI for the area between 0.53 and 0.69, P < 0.05) (Figure 1). The PNI cutoff value corresponded to a sensitivity value of 71.70% and a specificity value of 49.50%. For subsequent data analysis, the patients were divided into two groups according to the cutoff value for further analysis: the low-PNI group (PNI < 47.975) and high-PNI group (PNI ≥ 47.975).

Correlation of PNI with survival and prognosis assessment

Overall, the 1-, 2-, 3- and 5-year OS rates were 67.4%, 48.5%, 41.0% and 29.4%, respectively. No patients were lost to follow-up. For the patients with a PNI ≥ 47.975 (n =116), the 1-, 2-, 3- and 5-year OS rates were 74.1%, 56.7%, 47.7% and 36.9%, respectively, and the corresponding rates in the patients with a PNI < 47.975 (n = 77) were 57.10%, 36.2%, 31.2% and 16.5%, respectively. Kaplan–Meier analysis showed that, overall, the high-PNI group had OS superior to that of the low-PNI group (P = 0.001, Figure 2). According to different treatment processes, the mean pretreatment PNI, PNI during treatment, and post-treatment PNI values were 49.001 ± 4.680, 35.254 ± 4.664 and 39.915 ± 4.968, respectively (P < 0.001, Figure 3).

Univariate and multivariate survival analysis

The univariate analysis identified tumour length (P = 0.031), T-stage (P = 0.04), synchronous chemotherapy (P = 0.017) and PNI (P = 0.001) were significant prognostic factors associated with OS. From the multivariate analyses, we found that PNI (HR = 0.584; 95% CI = 0.408–0.835; P = 0.003), synchronous chemotherapy (HR = 0.511; 95%CI = 0.309–0.847; P = 0.009) and tumour length (HR = 1.558; 95%CI = 1.074–2.259; P = 0.019) were significant prognostic markers for OS (Table 2).

Toxicities

Table 3 summarises the haematological- and non-haematological-related adverse reactions observed during treatment. Overall, grade 3 or 4 adverse reactions in haematology were mainly seen in neutropenia, with 41 (35%) in the high-PNI group and 18 (23%) in the low-PNI group observed (P = 0.077). Grade 3 or 4 non-haematological adverse reactions were mainly seen in radiation esophagitis, with 12 (10%) in the high-PNI group and 11 (14%) in the low-PNI group observed (P = 0.408). However, there were no significant differences between adverse events after treatment between the two groups.

Discussion

Recently, many research studies have found that the PNI has an important role in cancer development and prognosis. However, to our knowledge, no studies have investigated the prognostic value of pretreatment PNI in ESCC patients who received radical RT with or without synchronous chemotherapy. We demonstrated the significant predictive value of PNI in ESCC patients who received radical CRT or RT. Our results showed that a high PNI (< 47.975 vs. ≥49.975) was significantly associated with decreased tumour length, T-stage and synchronous chemotherapy. Moreover, the low-PNI group was significantly associated with shorter OS in ESCC patients treated with radical CRT or RT, and pretreatment PNI was shown by multivariate analysis to be an independent prognostic factor.

The PNI, which is based on the serum albumin level and lymphocyte count, was originally proposed to assess risk and prognosis of patients undergoing gastrointestinal surgery [13]. In recent years, an increasing number of studies have used PNI to evaluate the prognosis of patients with malignant tumours and have found that it has nothing to do with the location and origin of the tumour [14]. Thereafter, the PNI can be used to assess the prognosis of tumours as follows: (I) Serum albumin pretreatment is of great value in tumour nutrition, and the PNI can contribute not only to understanding the nutritional status of patients but also be used to determine the albumin level, which is useful because the albumin level has been shown to have a negative correlation with cancer risk [16], so survival and prognosis of tumour patients can be predicted. (II) Tumour-related inflammation and malnutrition can inhibit albumin synthesis, whereas hypoalbuminemia can reflect the degree of inflammation and may negatively affect patient survival [17, 18]. (III) Low lymphocyte counts in cancer patients indicate an immunosuppressed state and can lead to poor prognosis [19]. (IV) In the process of tumour development, cancer cells can avoid and suppress the T-cell immune response in various ways [20, 21].

In recent years, several studies have begun to analyse the relationship between the PNI and prognosis in patients with oesophageal cancer. However, there is some controversy regarding the PNI in oesophageal cancer research. Han et al. [22] retrospectively analysed 206 patients with ESCC after esophagectomy and found that a high PNI had a positive effect on OS in patients with ECSS, but the PNI was not found to be an independent prognostic factor, which was not consistent with our finding that the PNI was significantly associated with the OS ($P = 0.002$) and therefore the prognosis of oesophageal cancer. Our multivariate analysis also showed that multiple variables were significantly associated with OS in oesophageal cancer, which was similar to the findings of Sun et al. [23]. The default PNI cutoff value is 50, which may deviate from the optimal PNI value for oesophageal cancer and influence the outcome of prognostic factors.

In addition, a study conducted by Nakatani et al. [24] in 66 patients with ESCC who received neoadjuvant chemotherapy found that patients with a PNI ≥ 45 had OS better than those with a PNI < 45 at 3 and 5 years (66.9%, 51.2% vs .33.3%, 0%, respectively), those with a PNI ≥ 45 had 3- and 5-year recurrence-free survival (RFS) rates better than those with a PNI < 45 (60.7%, 41.8% vs. 33.3%, 0%, respectively), and the preoperative PNI was an independent prognostic factor for OS and RFS. Hirahara et al. [25] conducted a retrospective study in 169 patients who underwent radical oesophageal cancer surgery and found that a PNI < 49.2 was an independent poor predictor of CSS and OS. In another retrospective study in 106 patients with cervical oesophageal cancer who underwent radiotherapy, Dai et al. [26] found significantly lower OS rates in the PNI < 48.15 group than in the PNI ≥ 48.15 group ($P = 0.004$). In the present study, the ROC curve was used to calculate the optimal PNI cutoff value, which was 47.975. The 5-year OS was significantly better in the ESCC patients with a pretreatment PNI ≥ 47.975 than in those with a PNI $<$ 47.975, and PNI was an independent prognostic factor in the multivariate analysis. We also analysed the change in PNI during the entire treatment process. The lowest PNI value in the treatment may be affected by various interventions. Oesophageal cancer is one of the most common cancers that cause malnutrition, and chemoradiation can lead to decreased appetite, obvious gastrointestinal reactions and myelosuppression. Inhibition may lead to a decrease in the PNI value.

In this study, we also found that PNI, tumour length and concurrent chemotherapy were independent prognostic factors in ESCC. The prognosis of ESCC tumours < 5 cm in length is significantly better than those ≥ 5 cm in length, which is consistent with the results of oesophageal cancer treated with proton radiation in another study [27]. In this study, the survival rate was better for patients who received concurrent chemotherapy than for those who did not (5-year OS: 32.4% vs. 0%, respectively). Chemotherapy has been previously shown to be associated with a favourable prognosis for oesophageal cancer [28].

This study had several limitations. First, this was a single-centre retrospective study with a small sample size. We were not able to demonstrate the effectiveness of PNI for predicting the prognosis of ESCC patients treated with CRT because of our sample size, so a large-sample prospective study is needed. Second, according to the PNI value we recorded throughout the treatment, but after the treatment, the PNI value showed a significant decline due to various factors, we had not found its value for prognosis. Finally, the AUC was relatively low, so a more sensitive prediction model needs to be constructed.

Conclusion

Among ESCC patients who underwent radical RT, PNI before treatment was found to be a nutrition-based prognostic factor. In clinical practice, the measurement of PNI is reliable, cheap and easy to obtain. For patients with low-PNI levels before treatment, nutritional intervention should be provided in a timely manner. Therefore, PNI will help clinical decision-making in tumour treatment options. Large-scale prospective studies are needed to verify the accuracy and practicality of the PNI.

List Of Abbreviations

CI Confidence interval

CRT Chemoradiotherapy

CT Computed tomography

CTV Clinical target volume

ESCC Oesophageal squamous cell carcinoma

GTV Gross tumour volume

HR Hazard ratio

KPS Karnofsky Performance Status

OS Overall survival

PNI Prognostic nutritional index

ROC Receiver operating characteristic

RT Radiotherapy

Declarations

Acknowledgements

Not applicable.

Authors' contributions

LX and JHL participated in the design. LX, XL, KL, YW, RKZ, and TYC

participated in data collection. LX, JHL, and TL participated in data analysis. All authors participated in data interpretation, drafting, and finalizing the report.

Corresponding author

Correspondence to Tao Li

Funding

Wu Jieping Medical Foundation, Grant/Award Number: 320.6750.17237.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The informed consent was waived because of the retrospective nature of the study.

Consent for publication

Not applicable.

Competing interests

All authors declare that they have no competing interests.

References

1. Siegel RL, Miller KD, Jemal A. Cancer Statistics, 2018. Ca-a Cancer Journal For Clinicians. 2018;68:7-30.
2. Lin Y, Totsuka Y, He Y, Kikuchi S, Qiao Y, Ueda J, et al. Epidemiology of esophageal cancer in Japan and China. J Epidemiol. 2013;23:233-42.
3. Huang FL, Yu SJ. Esophageal cancer: Risk factors, genetic association, and treatment. Asian J Surg. 2018;41:210-5.
4. Shitara K, Matsuo K, Hatooka S, Ura T, Takahari D, Yokota T, et al. Heavy smoking history interacts with chemoradiotherapy for esophageal cancer prognosis: a retrospective study. Cancer Sci. 2010;101:1001-6.
5. Pandeya N, Williams G, Green AC, Webb PM, Whiteman DC. Alcohol Consumption and the Risks of Adenocarcinoma and Squamous Cell Carcinoma of the Esophagus. Gastroenterology. 2009;136:1215-24.e2.
6. Bozzetti F, Mariani L, Lo Vullo S, Group SW, Amerio ML, Biffi R, et al. The nutritional risk in oncology: a study of 1,453 cancer outpatients. Support Care Cancer. 2012;20:1919-28.
7. Sun K, Chen S, Xu J, Li G, He Y. The prognostic significance of the prognostic nutritional index in cancer: a systematic review and meta-analysis. J Cancer Res Clin Oncol. 2014;140:1537-49.
8. Onodera T, Goseki N, Kosaki G. Prognostic nutritional index in gastrointestinal surgery of malnourished cancer patients. Nihon Geka Gakkai Zasshi. 1984;85:1001-5.
9. Wang D, Hu X, Xiao L, Long G, Yao L, Wang Z, et al. Prognostic nutritional index and systemic immune-inflammation index predict the prognosis of patients with hcC. J Gastrointest Surg. 2020.
10. Yang Y, Gao P, Chen X, Song Y, Shi J, Zhao J, et al. Prognostic significance of preoperative prognostic nutritional index in colorectal cancer: results from a retrospective cohort study and a meta-analysis. Oncotarget. 2016;7:58543-52.
11. Hubbard TJ, Lawson-McLean A, Fearon KC. Nutritional predictors of postoperative outcome in pancreatic cancer. Br J Surg. 2011;98:1032; author reply -3.
12. Nozoe T, Ninomiya M, Maeda T, Matsukuma A, Nakashima H, Ezaki T. Prognostic nutritional Index: A tool to predict the biological aggressiveness of gastric carcinoma. Surgery Today. 2010;40:440-3.
13. Smale BF, Mullen JL, Buzby GP, Rosato EF. The efficacy of nutritional assessment and support in cancer surgery. Cancer. 1981;47:2375-81.

14. Proctor MJ, Morrison DS, Talwar D, Balmer SM, Fletcher CD, O'Reilly DS, et al. A comparison of inflammation-based prognostic scores in patients with cancer. A Glasgow Inflammation Outcome Study. Eur J Cancer. 2011;47:2633-41.
15. Kim S, McClave SA, Martindale RG, Miller KR, Hurt RT. Hypoalbuminemia and Clinical Outcomes: What is the Mechanism behind the Relationship? American Surg. 2017;83:1220-7.
16. Wulaningsih W, Holmberg L, Garmo H, Malmstrom H, Lambe M, Hammar N, et al. Prediagnostic serum inflammatory markers in relation to breast cancer risk, severity at diagnosis and survival in breast cancer patients. Carcinogenesis. 2015;36:1121-8.
17. Suh B, Park S, Shin DW, Yun JM, Keam B, Yang HK, et al. Low albumin-to-globulin ratio associated with cancer incidence and mortality in generally healthy adults. Ann Oncol. 2014;25:2260-6.
18. Gupta D, Lis CG. Pretreatment serum albumin as a predictor of cancer survival: a systematic review of the epidemiological literature. Nutr J. 2010;9:69.
19. von Bernstorff W, Voss M, Freichel S, Schmid A, Vogel I, Johnk C, et al. Systemic and local immunosuppression in pancreatic cancer patients. Clin Cancer Res. 2001;7:925s-32s.
20. Whiteside TL. Tricks tumors use to escape from immune control. Oral Oncol. 2009;45:e119-23.
21. Kerkar SP, Restifo NP. Cellular constituents of immune escape within the tumor microenvironment. Cancer Res. 2012;72:3125-30.
22. Han L, Song Q, Jia Y, Chen X, Wang C, Chen P, et al. The clinical significance of systemic inflammation score in esophageal squamous cell carcinoma. Tumor Biol. 2016;37:3081-90.
23. Sun P, Zhang F, Chen C, An X, Li Y-H, Wang F-H, et al. Comparison of the prognostic values of various nutritional parameters in patients with esophageal squamous cell carcinoma from Southern China. J Thorac Dis. 2013;5:484-91.
24. Nakatani M, Migita K, Matsumoto S, Wakatsuki K, Ito M, Nakade H, et al. Prognostic significance of the prognostic nutritional index in esophageal cancer patients undergoing neoadjuvant chemotherapy. Dis Esophagus. 2017;30.
25. Hirahara N, Tajima Y, Fujii Y, Kaji S, Yamamoto T, Hyakudomi R, et al. Preoperative Prognostic Nutritional Index Predicts Long-Term Surgical Outcomes in Patients with Esophageal Squamous Cell Carcinoma. World J Surg. 2018;42:2199-208.
26. Dai Y, Fu X, Li T, Yao Q, Su L, Su H, et al. Long-term impact of prognostic nutritional index in cervical esophageal squamous cell carcinoma patients undergoing definitive radiotherapy. Ann Transl Med. 2019;7:175.
27. Tsunemoto H, Ishikawa T, Morita S, Kitagawa T, Tsujii H. Indications of particle radiation therapy in the treatment of carcinoma of the esophagus. Int J Radiat Oncol Biol Phys. 1992;22:321-4.
28. Stahl M, Stuschke M, Lehmann N, Meyer HJ, Walz MK, Seeber S, et al. Chemoradiation with and without surgery in patients with locally advanced squamous cell carcinoma of the esophagus. J Clin Oncol. 2005;23:2310-7.

Tables

Table 1 Basic and clinicopathological characteristics of 193 ESCC patients according to the pre-treatment PNI

Characteristics	Patients, n (%)	PNI < 47.975 (n=77)	PNI ≥ 47.975 (n=116)	P
Age (years)				0.719
<65	102 (52.85)	40	62	
≥65	91 (47.15)	37	54	
Sex				0.269
Male	149 (77.20)	60	89	
Female	44 (22.80)	17	27	
Smoking history				0.376
No	83 (43.01)	35	48	
Yes	110(56.99)	42	68	
Drinking history				0.885
No	83 (42.49)	33	50	
Yes	110 (56.99)	44	66	
KPS score				0.698
70	7 (3.63)	3	4	
80	96 (49.74)	35	62	
90	90 (46.63)	39	50	
Localisation				
Cervical	22 (11.40)	11	11	0.314
Upper thoracic	74 (38.34)	29	45	
Middle thoracic	83 (43.01)	30	53	
Lower thoracic	14 (7.25)	7	7	
Tumour length (cm)				0.035
<5.0	82 (42.49)	28	54	
≥5.0	111 (57.51)	49	62	
T-stage				0.007
T2	14 (7.25)	6	8	
T3	84 (43.52)	22	62	
T4	95 (49.22)	49	46	
N-stage				0.201
N0	1 (0.52)	1	0	
N1	73 (37.82)	28	45	
N2	88 (45.60)	32	56	
N3	31 (16.06)	16	15	
N3				
TNM stages				0.931
II	9 (4.66)	3	6	
III	184 (95.34)	74	110	
BMI (kg/m^2)				0.269

<23.0	138 (71.50)	58	80	
≥23.0	55 (28.50)	19	36	
RT dose (Gy)				0.14
<60	12 (6.22)	9	3	
≥60	181 (93.78)	68	113	
Chemotherapy				0.04
No	23 (11.92)	13	10	
Yes	170 (87.56)	64	106	

BMI, body mass index; RT, radiotherapy; PNI, prognostic nutritional index; ESCC, oesophageal squamous cell carcinoma.

Table 2 Univariate analysis of prognostic factors for OS in patients with ESCC

Characteristics	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P	HR (95% CI)	P
Age (years)				
<65	1		1	
≥65	1.306（0.920–1.853）	0.136	-	0.289
Sex				
Female	1		1	
Male	0.980(0.643–1.494)	0.926	-	0.997
Smoking history				
No	1		1	
Yes	1.151(0.807–1.643)	0.437	-	0.305
Drinking history				
No	1		1	
Yes	1.265(0.885–1.809)	0.197	-	0.134
KPS score				
70	1		1	
80	0.729(0.316–1.681)	0.729	-	0.261
90	0.573(0.246–1.339)	0.573	-	0.186
Localisation				
Cervical	1		1	
Upper thoracic	0.921(0.507–1.671)	0.786	-	0.790
Middle thoracic	0.971(0.539–1.749)	0.921	-	0.926
Lower thoracic	1.028(0.456–2.316)	0.947	-	0.843
Tumour length (cm)				
<5.0	1		1	
≥5.0	1.489 (1.038–2.136)	0.031	1.558 (1.074–2.259)	0.019
T-stage				
T2	1		1	
T3	0.999 (0.491–2.03)	0.997	-	0.353
T4	1.568 (0.780–3.153)	0.207	-	0.091
N-stage				
N0	1		1	
N1	0.441 (0.060–3.214)	0.419	-	0.129
N2	0.472 (0.065–3.427)	0.458	-	0.948
N3	0.798 (0.108–5.912)	0.825	-	0.039
TNM stage				
II	1		1	
III	1.785 (0.729–4.373)	0.205	-	0.084
BMI (kg/m^2)				

<23.0	1		1	
≥23.0	0.841 (0.569-1.242)	0.384	-	0.560
RT dose (Gy)				
<60	1		1	
≥60	1.052 (0.491-2.257)	0.896	-	0.499
Chemotherapy				
No	1		1	
Yes	0.552 (0.338-0.901)	0.017	0.511 (0.309-0.847)	0.009
PNI				
<47.975	1		1	
≥47.975	0.550 (0.386-0.785)	0.001	0.584 (0.408-0.835)	0.003

BMI, body mass index; RT, radiotherapy; PNI, prognostic nutritional index; ESCC, oesophageal squamous cell carcinoma; HR, hazard ratio; CI, confidence interval.

Table 3 Adverse events during chemoradiotherapy

Adverse reactions	PNI < 47.975 (n=77)	PNI ≥ 47.975 (n=116)	P
Neutropenia			
Any grade	53（69%）	94（81%）	0.051
≥Grade 3	18（23%）	41（35%）	0.077
Anaemia			
Any grade	60（78%）	72（62%）	0.022
≥Grade 3	7（9%）	6（5%）	0.288
Thrombocytopenia			
Any grade	44（57%）	65（56%）	0.879
≥Grade 3	6（8%）	16（14%）	0.199
Anorexia/Vomiting			
Any grade	67（87%）	103（89%）	0.709
≥Grade 3	0（0%）	1（1%）	0.414
Radiation oesophagitis			
Any grade	77（100%）	116（100%）	1.000
≥Grade 3	11（14%）	12（10%）	0.408
Radiation pneumonitis			
Any grade	74（14%）	107（92%）	0.263
≥Grade 3	6（8%）	6（5%）	0.465

PNI, prognostic nutritional index.

Figures

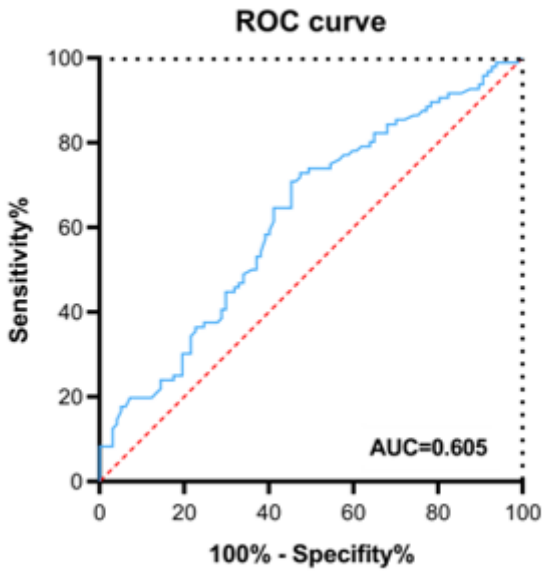

Figure 1

ROC curve for the PNI value for predicting the prognosis of ESCC. ROC, receiver operating characteristic; PNI, prognostic nutritional index; ESCC, oesophageal squamous cell carcinoma.

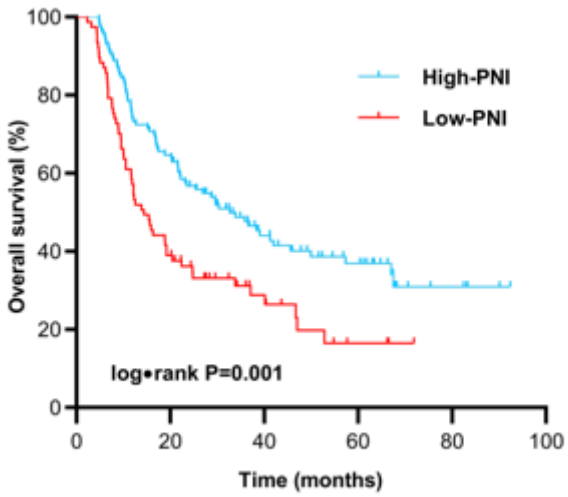

Figure 2

Kaplan–Meier survival curves for 193 ESCC patients according to cutoff values for the PNI. ESCC, oesophageal squamous cell carcinoma.

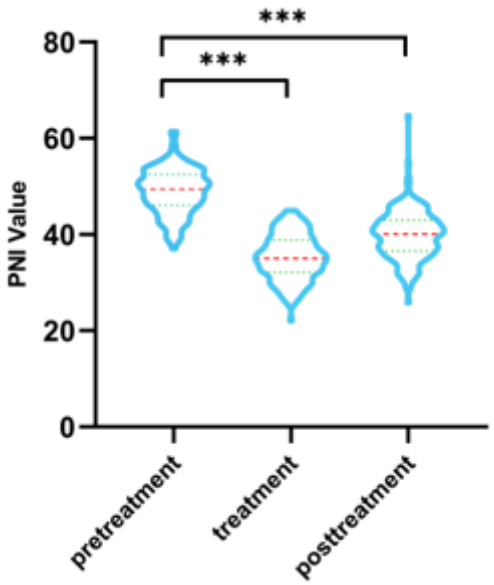

Figure 3

Changes in the PNI value during treatment. PNI, prognostic nutritional index.