Peertechz

International Journal of Radiology and Radiation Oncology
radiology@peertechz.us
CLINICAL GROUP

INTERNATIONAL JOURNAL OF Radiology and Radiation Oncology OPEN ACCESS JOURNAL

ISSN: 2640-7566 DOI: https://dx.doi.org/10.17352/ijrro

Research Article

Post-radiation Prognostic Nutritional Index Predicts Survival and Guides Consolidation Chemotherapy in Esophageal Cancer Patients

Xiaomei Zhou#, Xiangfei Wu#, Tongxin Liu, Shuimiao Lin, Ziyi Luo, Jingyi Wu, Rong Wang* and Wei Wang*

Department of Radiation Oncology, Nanfang Hospital, Southern Medical University, 1838, Guangzhou Avenue North, Guangzhou, 510515, People's Republic of China

#These authors contributed equally to this work

Received: 23 January, 2025
Accepted: 06 February, 2025
Published: 07 February, 2025

***Corresponding author:** Rong Wang, MD, PhD, Department of Radiation Oncology, Nanfang Hospital, Southern Medical University, 1838, Guangzhou Avenue North, Guangzhou, 510515, People's Republic of China, E-mail: 836590644@qq.com

Wei Wang, MD, PhD, Department of Radiation Oncology, Nanfang Hospital, Southern Medical University, 1838, Guangzhou Avenue North, Guangzhou, 510515, People's Republic of China, E-mail: wangwei9500@hotmail.com

Keywords: Esophageal Cancer; Definitive chemoradiotherapy; Prognostic nutritional index; Consolidation chemotherapy; Survival analysis

https://www.cancerresgroup.us

Check for updates

Abstract

Purpose: Nutritional status is associated with the prognosis of esophageal cancer (EC) patients, which can influence treatment efficacy. Additionally, the efficacy of consolidation chemotherapy (CCT) after definitive chemoradiotherapy (DCRT) is unclear. This study aimed to explore the prognostic value of the prognostic nutritional index (PNI) at different treatment periods, as well as its influence on CCT efficacy.

Methods: We reviewed the data of 106 patients with cT2-4N0-3M0 EC who received DCRT between December 2016 and October 2020. Survival analyses were performed to investigate the prognostic effect of PNI and CCT.

Results: The 3-year Progression-Free Survival (PFS) and Overall Survival (OS) rates were 41.58% and 49.31%, respectively. In the univariate analysis, tumor location, T stage, N stage, clinical stage, and post-radiation PNI were significantly associated with PFS, whereas tumor location, N stage, clinical stage, CCT, and post-radiation PNI were associated with OS. Furthermore, post-radiation PNI was identified as an independent risk indicator for PFS and OS, and CCT was identified as an independent risk indicator for OS by multivariate analysis. Additionally, we found that PNI detected 60–120 days after radiotherapy may be an ideal prognostic predictor. CCT improved PFS and OS in patients with post-radiation PNI ≥ 41.98, but not in patients with post-radiation PNI < 41.98.

Conclusion: Our results revealed that post-radiation PNI and CCT were independently associated with survival in EC patients receiving DCRT. However, patients with low post-radiation PNI could not benefit from CCT, indicating that it is unnecessary to add CCT after concurrent chemoradiotherapy in these patients.

Introduction

Esophageal cancer (EC) is the eleventh most frequently diagnosed cancer and the seventh leading cause of cancer-related death worldwide [1]. For patients with locally advanced unresectable esophageal cancer, definitive chemoradiotherapy (DCRT) is recommended as the preferred treatment option [2], which can result in a 5-year Overall Survival (OS) rate of 26% – 44.3% [3,4]. However, the clinical application of DCRT has certain limitations because of its high risk of adverse events and the poor nutritional status of EC patients. It was reported that some EC patients have poor tolerance to DCRT because of poor basal nutritional status [5,6]. These patients not only fail to benefit from treatment but also experience increased physical toxicity and economic burden. Concurrent chemoradiotherapy followed by Consolidation Chemotherapy

Citation: Zhou X, Wu X, Liu T, Lin S, Luo Z, Wu J, et al. Post-radiation Prognostic Nutritional Index Predicts Survival and Guides Consolidation Chemotherapy in Esophageal Cancer Patients. Int J Radiol Radiat Oncol. 2025;11(1): 001-008. DOI: https://dx.doi.org/10.17352/ijrro.000054

(CCT) is the commonly used treatment strategy for DCRT, but the effect of CCT on EC patients remains controversial. Which type of EC patients can benefit from CCT, and can nutritional status guide the application of CCT? This is worthy of further exploration.

There is no doubt that nutritional status is an important prognostic factor for EC patients. The prognostic nutritional index (PNI), calculated by the serum albumin concentration and total lymphocyte count in peripheral blood, was reported as a prognostic predictor in several types of tumors, including EC, breast cancer, melanoma, and so on [7-10]. However, most of these current studies focused only on the prognostic value of baseline PNI, without exploring the prognostic value of PNI at different treatment periods. In addition, previous studies regarding prognostic factors came to different conclusions, possibly because the factors included in the analysis were not comprehensive enough [11-14].

Therefore, we collected clinical data, including PNI at different treatment periods, to investigate the prognostic value of PNI and CCT in EC patients receiving DCRT from multiple dimensions.

Methods

Patients and clinical data

This retrospective study of outcomes after DCRT in EC patients was approved by the Research Ethics Committee of our hospital. Between December 2016 and October 2020, 481 EC patients received radiotherapy at our institution. We excluded 351 patients who did not receive DCRT and 24 patients without complete medical records. Thus, 106 patients with clinical stages of cT2-4N0-3M0 were enrolled in the study. All patients were ≥18 years of age, had histologically confirmed EC without distant metastases, received DCRT, and had complete survival and treatment information. Patients with distant metastasis, second primary tumor, or incomplete DCRT were excluded.

We retrospectively collected several clinical characteristics of patients, including age, sex, smoking history, alcohol use, baseline PNI, post-radiation PNI, PNI change, histological type, tumor location, clinical TNM stage, tumor length, gross tumor volume (GTV), radiation dose and number of chemotherapy cycles. The PNI was calculated as 10 × serum albumin (g/dL) + 0.005 × total lymphocyte count (per mm^3). PNI change was defined as the baseline PNI minus the post-radiation PNI. Tumor location was determined by endoscopy. A tumor 15 cm to 20 cm away from the superior incisor was defined as cervical, whereas tumors 20 cm to 25 cm, 25 cm to 30 cm, and 30 cm to 40 cm were defined as upper thoracic, middle thoracic, and lower thoracic, respectively. The stage of EC was determined based on the eighth edition of the American Joint Committee of Cancer (AJCC) TNM staging system for EC. CCT was defined as chemotherapy after concurrent chemoradiotherapy which was decided to be conducted according to the patient's degree of tolerance to chemotherapy, patient willingness, efficacy of DCRT, and other comprehensive factors.

The protocol of definitive chemoradiotherapy

All patients received external beam radiation using intensity-modulated radiation therapy. We determined the GTV of the primary tumor (GTVp) using the borders of the primary esophageal tumor based on imaging examination. GTV of lymph nodes (GTVn) was defined by the enlarged regional lymph nodes, i.e., lymph nodes with short diameter ≥ 1 cm (paraesophageal or tracheoesophageal groove ≥ 5 mm) on computed tomography or endoscopic ultrasound, or lymph nodes with high standardized uptake value (except for inflammatory lymph nodes) on 18F-fluorodeoxyglucose-positron emission tomography/computed tomography. The GTV consisted of GTVp and GTVn, which were calculated in cubic centimeters (cc) using the Varian Eclipse system. The clinical target volume included a 3 cm craniocaudal and a 0.5–0.8 cm radial margin around the GTVp, and a 1-cm craniocaudal and a 0.5–0.8 cm radial margin around the GTVn, which included the area of subclinical involvement. The planning target volume was determined by including an area of 0.5 cm around the clinical target volume in all directions of tumor motion and setup variations. All plans were optimized such as D95 (DV is the absorbed dose in V% of the volume) ≥ the prescription dose and D1cc ≤ 115% of the prescription dose. The normal tissue-dose constraints included Dmax < 45 Gy for the spinal cord, V30 < 45% for the heart, V20 < 25% for the lung, Dmax < 45 Gy for the intestine, and V30 < 30% for the liver.

During radiotherapy, chemotherapy was administered with either paclitaxel and platinum every three weeks or fluoropyrimidine and platinum every four weeks for 2 cycles. The CCT regimen was the same as the concurrent chemoradiotherapy, which was administered three weeks or four weeks after the last concurrent chemotherapy for 2–4 cycles. During DCRT and CCT, oral nutritional supplementation was preferred for EC patients with insufficient nutritional intake and tube feeding was selected for patients with high-risk factors such as moderate-severe dysphagia and severe chemoradiotherapy esophageal mucositis affecting oral feeding. When enteral nutrition could not meet the patient's nutritional needs, enteral nutrition combined with partial parenteral nutrition or total parenteral nutrition was selected.

Follow up

Patients were regularly followed up in the outpatient clinic or using telephone interviews. Clinical evaluations included a computed tomography scan of the neck-, thorax-, and abdomen performed every 3 to 6 months. Endoscopic examination and bone scan were performed to detect recurrence and metastasis when necessary. OS was defined as the interval from the beginning day of DCRT to the date of death or last follow-up. Progression-Free Survival (PFS) was calculated from the beginning day of DCRT until disease progression or death. Patients who were still alive or lost to follow-up were considered as censored data for analysis of survival rates.

Statistical analysis

The statistical analyses were performed using SPSS software (version 23.0; IBM Corp., Armonk, NY, USA) and GraphPad

Citation: Zhou X, Wu X, Liu T, Lin S, Luo Z, Wu J, et al. Post-radiation Prognostic Nutritional Index Predicts Survival and Guides Consolidation Chemotherapy in Esophageal Cancer Patients. Int J Radiol Radiat Oncol. 2025;11(1): 001-008. DOI: https://dx.doi.org/10.17352/ijrro.000054

Prism 8.0 software (GraphPad, La Jolla, CA, USA). Categorical variables were presented as numbers and percentages, and groups were compared using the χ^2 test or nonparametric methods, such as the Mann-Whitney test. Continuous variables were expressed as the means and standard deviations, and means were compared using *Student's t*-test. Time-dependent Receiver Operating Characteristic (ROC) curve analysis was used to identify the optimal cut-off values of baseline PNI, post-radiation PNI, PNI change, tumor length, and GTV for predicting 15-month OS and to compare their predictive capacity. The survival time distribution was evaluated using the Kaplan-Meier method, and the log-rank test was used for comparisons. A multivariate Cox proportional hazard model was used to identify independent prognostic markers. A two-tailed $p < 0.05$ was considered statistically significant.

Results

Patient and tumor characteristics

To investigate the prognostic factors for EC patients receiving DCRT, we reviewed the data of 106 patients fulfilling the study's eligibility criteria between 2016 and 2020 (Supplementary Figure 1). The collected information included age, sex, smoking history, alcohol use, baseline PNI, post-radiation PNI, PNI change, histology, tumor location, T stage, N stage, clinical stage, tumor length, GTV, radiation dose, and CCT. As shown in Table 1, a majority of patients were males (79.2%) with esophageal squamous cell carcinoma (88.7%), and nearly half of the patients had a history of smoking (56.6%) and alcohol use (44.3%). More than half of the cancers were located in the upper (38.7%) and middle (28.3%) esophagus, and the most common stages were T3 (67.0%) and N1-2 (67.0%). Most patients had locally advanced EC, i.e., stage III (50.9%) and IV (30.2%). In this study, most patients received DRCT with a radiation dose of no less than 60 Gy (62.3%), and over half of the patients (54.8%) received CCT.

In addition, we also collected information reflecting nutritional status, including baseline PNI (mean: 47.57), post-radiation PNI (mean: 44.11), and PNI change (mean: 4.19), and summarized information regarding tumor burden, including GTV (mean: 70.84 cm^3) and tumor length (mean: 5.62 cm). Using the ROC analysis method, we determined the optimal cut-off values to be 47.95, 41.98, 4.97, 59.55 cm^3, and 5.60 cm for baseline PNI, post-radiation PNI, PNI change, GTV, and tumor length, respectively (Supplementary Figure 2). Then, patients were divided into two groups based on the optimal cut-off values for further analysis.

Univariate and multivariate analyses of OS and PFS

The 3-year PFS rate was 41.58% with a median PFS of 24 months, and the 3-year OS rate was 49.31% with a median OS of 29 months (Supplementary Figure 3A and 3B). Univariate analyses were performed using the abovementioned clinical features (Tables 2,3). The results showed that tumor location (p = 0.006), T stage (p = 0.014), N stage (p = 0.018), clinical stage (P = 0.003) and post-radiation PNI (p = 0.011) were significantly associated with PFS, and that tumor location (p = 0.002), N stage (p = 0.043), clinical stage (p = 0.026), CCT (p = 0.008) and post-radiation PNI (p < 0.001) were significantly associated with OS. More importantly, multivariate Cox regression analysis showed that post-radiation PNI was identified as an independent risk indicator for PFS (Hazard Ratio (HR): 0.391, 95% Confidence Interval (CI): 0.177–0.862, p = 0.020) and OS (HR: 0.309, 95% CI: 0.116–0.823, p = 0.019), while CCT was identified as an independent risk indicator for OS (HR: 0.383, 95% CI: 0.150–0.978, p = 0.045) (Tables 2,3).

As shown by the Kaplan-Meier survival curves, patients with post-radiation PNI ≥ 41.98 were associated with better PFS (p = 0.011) and better OS (p < 0.001) (Figure 1A and 1D). However,

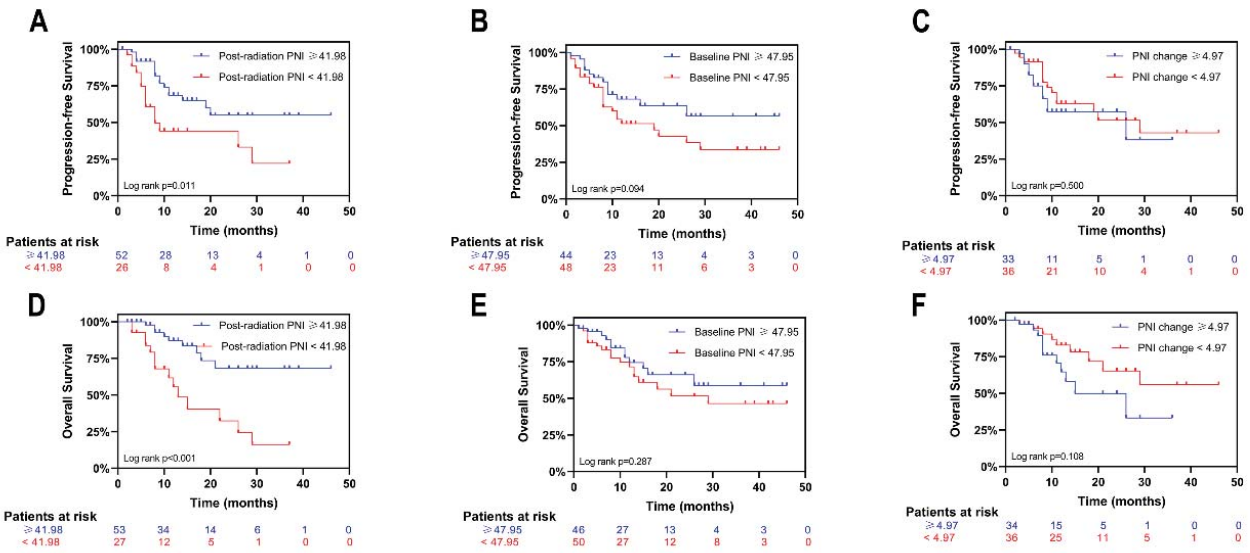

Figure 1: Kaplan-Meier curves for progression-free survival and overall survival stratified by PNI. Curves are shown for progression-free survival stratified by (A) post-radiation PNI, (B) baseline PNI, and (C) PNI change. Curves are shown for overall survival stratified by (D) post-radiation PNI, (E) baseline PNI, and (F) PNI change. PNI, prognostic nutritional index.

Citation: Zhou X, Wu X, Liu T, Lin S, Luo Z, Wu J, et al. Post-radiation Prognostic Nutritional Index Predicts Survival and Guides Consolidation Chemotherapy in Esophageal Cancer Patients. Int J Radiol Radiat Oncol. 2025;11(1): 001-008. DOI: https://dx.doi.org/10.17352/ijrro.000054

Table 1: Patients and treatment characteristics.

Variables	Study Cohort (*n* = 106) [a]
Age (yr) [b]	61.79 ± 11.05
Sex	
Male	84 (79.2)
Female	22 (20.8)
Smoking history	
Yes	60 (56.6)
No	46 (43.4)
Alcohol use	
Yes	47 (44.3)
No	59 (55.7)
Histology	
SCC	94 (88.7)
Others	12 (11.3)
Location	
Cervical	17 (16.1)
Upper thoracic	24 (22.6)
Middle thoracic	30 (28.3)
Lower thoracic	23 (21.7)
Others	12 (11.3)
T stage	
T2	6 (5.6)
T3	71 (67.0)
T4	25 (23.6)
Unknown	4 (3.8)
N stage	
N0	20 (18.8)
N1	30 (28.3)
N2	41 (38.7)
N3	13 (12.3)
Unknown	2 (1.9)
Clinical stage	
II	16 (15.1)
III	54 (50.9)
IVA	32 (30.2)
Unknown	4 (3.8)
Length (cm) [b]	5.62 ± 2.46
GTV (cm^3) [b]	70.84 ± 53.46
PNI	
Baseline PNI [b]	47.57 ± 5.44
Post-radiation PNI [b]	44.11 ± 5.32
PNI change [b]	4.19 ± 6.91
Radiation dose	
≥ 60 Gy	66 (62.3)
< 60 Gy	40 (37.3)
CCT	
Yes	57 (54.8)
No	49 (46.2)

Abbreviations: SCC: Squamous Cell Carcinoma; GTV: Gross Tumor Volume; PNI: Prognostic Nutritional Index; CCT: Consolidation Chemotherapy.
[a]Except where indicated, data are numbers of patients (%).
[b]Data are mean ± standard deviation (SD).

neither baseline PNI (Figure 1B and 1E) nor PNI change (Figure 1C and 1F) can predict PFS or OS. The results above indicated that post-radiation PNI and CCT were significant prognostic factors for EC patients undergoing DCRT. But how can the optimal time to detect PNI after DCRT be determined? Further analysis (Supplementary Figure 4) showed that post-radiation PNI could not predict PFS and OS when detected within 60 days after radiotherapy, but was associated with prognosis when detected 60–120 days after radiotherapy. PNI detected 60–120 days after radiotherapy may be an ideal prognostic predictor.

Correlation between post-radiation PNI and clinical characteristics

Then, we investigated the relationships between PNI and other clinical characteristics. As shown in Supplementary Table 1, there was a significant difference in smoking history between post-radiation PNI ≥ 41.98 and post-radiation PNI < 41.98 groups (p = 0.030). Otherwise, no significant differences were observed in terms of sex, age, histology, tumor location, T stage, N stage, clinical stage, tumor length, GTV, radiation dose, and CCT, which suggests that the two groups were well-balanced for analysis.

Survival analyses of interactions between post-radiation PNI and other variables

To determine whether the prognostic effect of post-radiation PNI on OS was influenced by any of the other clinical and treatment variables, we performed a subgroup analysis. Figure 2 shows that the benefit of post-radiation PNI ≥ 41.98 concerning overall survival was evident in the subgroups examined, including age, sex, smoking history, alcohol use, location, T stage, N stage, clinical stage, length, GTV, and radiation dose (P > 0.050 for all interactions). Interestingly, we found a potential modifying effect of CCT (p = 0.043 for

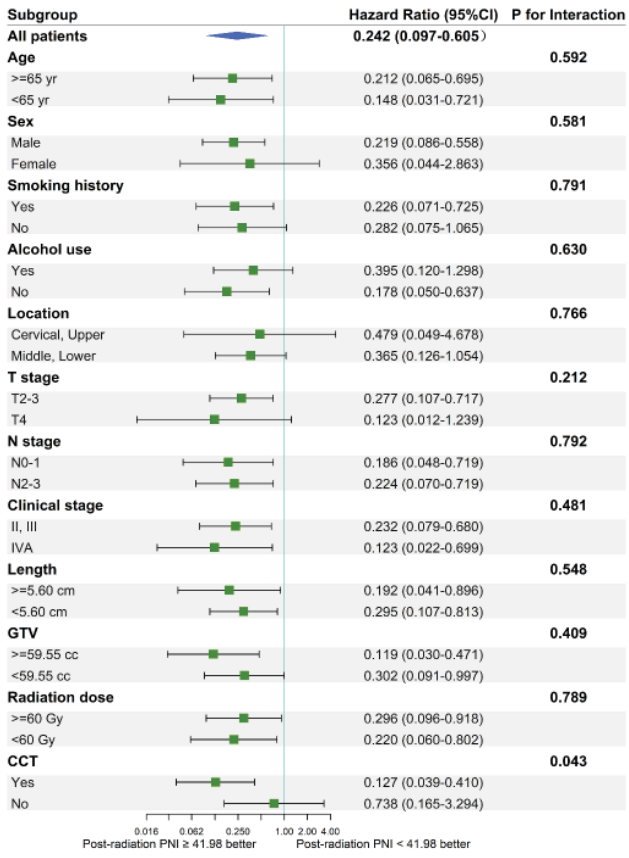

Figure 2: Subgroup analysis of overall survival. Shown are the results of subgroup analyses of the post-radiation PNI effect on overall survival. Hazard ratios for death in the group with post-radiation PNI of more than 41.98, as compared with the group with post-radiation PNI of less than 41.98, are shown along with 95% confidence intervals. PNI, prognostic nutritional index; 95% CI, 95% confidence interval; GTV, gross tumor volume; CCT, consolidation chemotherapy; cc, cubic centimeters.

Citation: Zhou X, Wu X, Liu T, Lin S, Luo Z, Wu J, et al. Post-radiation Prognostic Nutritional Index Predicts Survival and Guides Consolidation Chemotherapy in Esophageal Cancer Patients. Int J Radiol Radiat Oncol. 2025;11(1): 001-008. DOI: https://dx.doi.org/10.17352/ijrro.000054

Table 2: Univariate and multivariate analysis of progression-free survival.

Variables	Univariate analysis		Multivariate analysis	
	HR (95% CI)	*p*	HR (95% CI)	*p*
Age (≥ 65 *vs.* < 65 yr)	0.942 (0.530–1.676)	0.838		
Sex (male *vs.* female)	1.254 (0.635–2.477)	0.533		
Smoking (yes *vs.* no)	1.572 (0.882–2.801)	0.123		
Alcohol use (yes vs no)	1.355 (0.742–2.471)	0.295		
Location (cervical, upper *vs.* middle, lower)	0.397 (0.210–0.749)	0.006	-	0.325
T stage (T2-3 *vs.* T4)	0.459 (0.206–1.026)	0.014	-	0.284
N stage (N0-1 *vs.* N2-3)	0.489 (0.255–0.940)	0.018	-	0.680
Clinical stage (II-III *vs.* IVA)	0.389 (0.171–0.882)	0.003	-	0.057
Length (≥ 5.60 *vs.* < 5.60 cm)	1.326 (0.707–2.489)	0.354		
GTV (≥ 59.55 *vs.* < 59.55 cm^3)	1.760 (0.964–3.241)	0.053		
Baseline PNI (≥ 47.95 *vs.* < 47.95)	0.579 (0.306–1.094)	0.094		
Post-radiation PNI (≥ 41.98 *vs.* < 41.98)	0.417 (0.186–0.936)	0.011	0.391 (0.177–0.862)	0.020
PNI change (≥ 4.97 *vs.* < 4.97)	1.292 (0.589–2.834)	0.500		
Radiation dose (≥ 60 *vs.* < 60 Gy)	0.981 (0.532–1.809)	0.949		
CCT (yes *vs.* no)	0.608 (0.335–1.102)	0.094		

Abbreviations: HR: Hazard Ratio; 95% CI: 95% confidence interval; GTV: Gross Tumor Volume; PNI: Prognostic Nutritional Index; CCT: Consolidation Chemotherapy.

Table 3: Univariate and multivariate analysis of overall survival.

Variables	Univariate analysis		Multivariate analysis	
	HR (95% CI)	*p*	HR (95% CI)	*p*
Age (≥ 65 *vs.* < 65 yr)	1.411 (0.731–2.725)	0.294		
Sex (male *vs.* female)	0.867 (0.396–1.897)	0.707		
Smoking (yes *vs.* no)	1.317 (0.679–2.555)	0.412		
Alcohol use (yes *vs.* no)	1.783 (0.898–3.537)	0.078		
Location (cervical, upper *vs.* middle, lower)	0.287 (0.142–0.581)	0.002	-	0.364
T stage (T2-3 *vs.* T4)	0.558 (0.219–1.422)	0.222		
N stage (N0-1 *vs.* N2-3)	0.498 (0.247–1.004)	0.043	-	0.195
Clinical stage (II-III *vs.* IVA)	0.378 (0.160–0.889)	0.026	-	0.054
Length (≥ 5.60 *vs.* <5.60 cm)	1.057 (0.517–2.160)	0.877		
GTV (≥ 59.55 *vs.* < 59.55 cm^3)	1.634 (0.813–3.285)	0.148		
Baseline PNI (≥ 47.95 *vs.* < 47.95)	0.677 (0.331–1.385)	0.287		
Post-radiation PNI (≥ 41.98 *vs.* < 41.98)	0.242 (0.097–0.605)	< 0.001	0.309 (0.116–0.823)	0.019
PNI change (≥ 4.97 *vs.* < 4.97)	1.997 (0.809–4.926)	0.108		
Radiation dose (≥ 60 *vs.* < 60 Gy)	0.908 (0.456–1.809)	0.777		
CCT (yes *vs.* no)	0.403 (0.206–0.785)	0.008	0.383 (0.150–0.978)	0.045

Abbreviations: HR: Hazard Ratio; 95% CI: 95% Confidence Interval; GTV: Gross Tumor Volume; PNI: Prognostic Nutritional Index; CCT: Consolidation Chemotherapy

interaction) on the correlation between post-radiation PNI and OS.

Survival analysis of post-radiation PNI and consolidation chemotherapy

Finally, we combined post-radiation PNI and treatment information for a comprehensive survival analysis. Surprisingly, it is shown in Figure 3 that CCT could significantly improve the PFS and OS in EC patients with high post-radiation PNI (≥ 41.98), but not in patients with low post-radiation PNI (< 41.98) (Figure 3A and 3B). These results suggested that post-radiation PNI was associated with the efficacy of chemotherapy. It is important and necessary to perform nutrition monitoring and nutrition support during treatment for EC patients receiving DCRT.

Discussion

In the present study, post-radiation PNI with a cut-off value of 41.98 and CCT were identified as independent prognostic factors of EC patients receiving DCRT. Additionally, the optimal time to detect PNI may be 60–120 days after radiotherapy. Notably, patients with low post-radiation PNI (< 41.98) could not benefit from CCT. The results showed in our study that the 3-year OS rate was 49.31%. However, a phase III clinical trial in China [4] reported that the 3-year and 5-year OS rates were up to 55.4% and 44.3%, respectively, in locally advanced EC patients treated with DCRT. After further analysis, we found that 79.3% of patients completed at least one cycle of CCT in this phase III clinical trial. In our study, only 54.8% of the patients received at least one cycle of CCT. It seems that patients in this phase III clinical trial received higher-intensity therapy. Moreover, our study was a real-world retrospective study with most of the patients in poor general condition and adherence. In contrast, patients selected in the prospective clinical study were in good general condition due to the strict inclusion and exclusion criteria.

EC patients, especially those with locally advanced disease, are at a high risk of malnutrition because of dysphagia, odynophagia, anorexia, and so on [15-18]. The Nutrition Risk Screening 2002 (NRS-2002) [19-21] and Patient-Generated Subjective Global Assessment (PG-SGA) [22,23] have been widely used for nutritional assessment. However, these

Citation: Zhou X, Wu X, Liu T, Lin S, Luo Z, Wu J, et al. Post-radiation Prognostic Nutritional Index Predicts Survival and Guides Consolidation Chemotherapy in Esophageal Cancer Patients. Int J Radiol Radiat Oncol. 2025;11(1): 001-008. DOI: https://dx.doi.org/10.17352/ijrro.000054

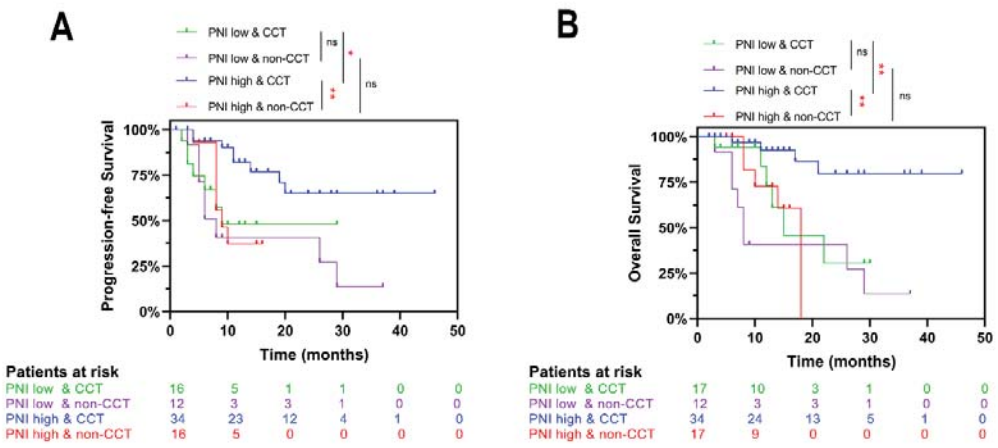

Figure 3: Kaplan-Meier curves for progression-free survival and overall survival stratified by post-radiation PNI and consolidation chemotherapy. Curves are shown for (A) progression-free survival and (B) overall survival stratified by post-radiation PNI and CCT. ns, $p > 0.05$, * $p < 0.05$, ** $p < 0.01$ by log-rank test. PNI, prognostic nutritional index; CCT, consolidation chemotherapy.

nutrition assessment methods are greatly subjective with a high workload, which has some limitations in this study. PNI, which quantifies the nutritional and immune status of patients to some extent, is a simple and useful survival indicator. Okadome et al. suggested that pre-treatment PNI was associated with the local immune response and survival of EC patients [7]. Nakatani, et al. found that baseline PNI was a useful marker for predicting clinical outcomes [24]. In contrast to previous studies, we further explored the prognostic value of PNI at different treatment periods and found that post-radiation PNI was superior to baseline PNI or PNI change in predicting the outcomes of EC patients undergoing DCRT. This result indicated that the nutritional status of patients after DRCT deserves our close attention. Timely nutritional support therapy should be provided for patients with lower post-radiation PNI. It is interesting that why post-radiation PNI affects survival, PNI change does not. It is easy to understand why this may be the case. The PNI change is defined as the baseline PNI minus the post-radiation PNI, which can only reflect the changing trend of PNI before and after radiotherapy but not the nutritional status of the patients at some time. Even though patients have the same values of PNI change, there may be an enormous difference in the values of their baseline PNI or post-radiation PNI. Therefore, post-radiation PNI, which reflects the nutritional and immune status after radiotherapy, rather than PNI change is an essential prognostic factor of EC patients receiving DCRT.

In this study, the post-radiation PNI was measured within 120 days after DCRT because the post-radiation PNI data at a fixed period were hard to collect in a retrospective study. The time of evaluation of PNI may change the PNI. Therefore, we preliminarily explored the appropriate detection time of post-radiation PNI and found that PNI detected 60–120 days after radiotherapy may be able to better predict the prognosis of EC patients. At 60 to 120 days after DCRT, almost all patients had finished the full course of DCRT and CCT. In this period, the PNI values are relatively stable and do not fluctuate greatly with treatment, which makes it a useful indicator.

According to the results of the RTOG 85-01 [3] and PRODIGE5/ACCORD17 [25] trials, the National Comprehensive Cancer Network (NCCN) guidelines recommend concurrent chemoradiotherapy combined with CCT as the standard treatment regimen for DCRT. However, the reason why CCT is added to DCRT has not been clarified, and the prognostic impact of CCT after concurrent chemoradiotherapy on EC patients remains controversial. It was reported in a retrospective study [26] that CCT did not improve PFS and OS in EC patients, whereas Xia, et al. [27] suggested that CCT significantly prolonged PFS and OS in EC patients. Our results showed that patients treated with CCT had longer OS. CCT is necessary for EC patients undergoing DCRT.

Malnutrition may reduce the sensitivity of chemoradiotherapy, increase the side effects, and decrease the treatment effect and quality of life [28,29]. Similarly, we found that EC patients with post-radiation PNI ≥ 41.98 could benefit from CCT, but patients with post-radiation PNI < 41.98 could not benefit from CCT, which indicated that post-radiation PNI was significantly associated with the treatment response. For patients with post-radiation PNI < 41.98, the choice of CCT should be approached with caution, because it did not improve the prognosis but instead increased the risk of toxic side effects as well as their economic burden. Thus, it is necessary to pay close attention to post-radiation PNI and take effective intervention measures in time to improve treatment efficacy.

However, our study also has the limitations inherent to retrospective observational studies. On the one hand, this was a retrospective study performed at a single institution; therefore, the results are waiting to be verified by prospective clinical trials. On the other hand, there were many other reported nutritional indices currently, such as neutrophil-lymphocyte count ratio (NLR), controlling nutritional status score (CONUT), nutritional risk index (NRI), systemic immune-inflammatory index (SII), body mass index (BMI), and so on. It was reported that NRI and coNRI-NLR models may be important prognostic

Citation: Zhou X, Wu X, Liu T, Lin S, Luo Z, Wu J, et al. Post-radiation Prognostic Nutritional Index Predicts Survival and Guides Consolidation Chemotherapy in Esophageal Cancer Patients. Int J Radiol Radiat Oncol. 2025;11(1): 001-008. DOI: https://dx.doi.org/10.17352/ijrro.000054

factors among immune indicators (including PNI, NRI, NLR, and SII) [30]. Yi-Shen Mao, et al. [31] suggested that CONUT might have a higher sensitivity and specificity in predicting complications and survival compared with PNI. Jinyu Shi, et al. [32] showed that PNI showed the highest predictive ability for patient prognosis among the nutritional assessments (including patient-generated subjective nutrition assessment (PGSGA), global leadership initiative on malnutrition (GLIM), CONUT, NRI, and PNI). Therefore, different studies have reached different conclusions. We did not compare the predictive ability of PNI with other well-established nutritional indices, which is the work we will focus on next.

Conclusion

This study identified post-radiation PNI instead of baseline PNI or PNI changes as an independent prognostic factor for long-term survival in EC patients receiving DCRT. In addition, patients treated with CCT were associated with longer survival, but those with low post-radiation PNI could not benefit from CCT. These findings emphasize that it is important and necessary for esophageal cancer patients to perform nutritional monitoring and management during DCRT.

Acknowledgment

We would like to express our sincere thanks to the Department of Radiation Oncology, Nanfang Hospital, and Southern Medical University.

Statements and declarations

Funding

This work was supported by the National Natural Science Foundation of China (grant number 82172642); the Outstanding Youths Development Scheme of Nanfang Hospital, Southern Medical University (grant number 2021J007); the GuangDong Basic and Applied Basic Research Foundation (grant number 2019A1515110931); and the President Foundation of Nanfang Hospital, Southern Medical University (grant number 2019L001).

Author's contributions

XZ, RW, and WW contributed to the study conception and design. Material preparation and data collection were performed by TL, SL, ZL, and JW. XZ and XW analyzed and interpreted the data. The first draft of the manuscript was written by XZ and XW. WW revised the manuscript. All authors read and approved the final manuscript.

Ethics approval

This study involving human participants was performed in line with the principles of the Declaration of Helsinki and approved by the Research Ethics Committee of Nanfang Hospital, Southern Medical University (IRB number: NFEC-2021-390). Written informed consent for patients was not required for this study following the national legislation and the institutional requirements.

Data availability

The data presented in this study are available from the corresponding author upon reasonable request.

(Supplementary)

References

1. Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2024;74(3):229-63. Available from: https://doi.org/10.3322/caac.21834

2. Ajani JA, D'Amico TA, Bentrem DJ, Cooke D, Corvera C, Das P, et al. Esophageal and Esophagogastric Junction Cancers, Version 2.2023, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw. 2023;21:393-422. Available from: https://doi.org/10.6004/jnccn.2023.0019

3. Cooper JS, Guo MD, Herskovic A, Macdonald JS, Martenson JA, Jr., Al-Sarraf M, et al. Chemoradiotherapy of locally advanced esophageal cancer: long-term follow-up of a prospective randomized trial (RTOG 85-01). Radiation Therapy Oncology Group. JAMA. 1999;281:1623-7. Available from: https://doi.org/10.1001/jama.281.17.1623

4. Chen Y, Ye J, Zhu Z, Zhao W, Zhou J, Wu C, et al. Comparing Paclitaxel Plus Fluorouracil Versus Cisplatin Plus Fluorouracil in Chemoradiotherapy for Locally Advanced Esophageal Squamous Cell Cancer: A Randomized, Multicenter, Phase III Clinical Trial. J Clin Oncol. 2019;37:1695-703. Available from: https://doi.org/10.1200/JCO.18.02122

5. Wang B, Jiang X, Tian D, Geng W. Enteral nutritional support in patients undergoing chemoradiotherapy for esophageal carcinoma. Future Oncol. 2020;16:2949-57. Available from: https://doi.org/10.2217/fon-2020-0181

6. Lyu J, Li T, Xie C, Li J, Xing L, Zhang X, et al. Enteral nutrition in esophageal cancer patients treated with radiotherapy: a Chinese expert consensus 2018. Future Oncol. 2019;15:517-31. Available from: https://doi.org/10.2217/fon-2018-0697

7. Okadome K, Baba Y, Yagi T, Kiyozumi Y, Ishimoto T, Iwatsuki M, et al. Prognostic Nutritional Index, Tumor-infiltrating Lymphocytes, and Prognosis in Patients with Esophageal Cancer. Ann Surg. 2020;271(4):693-700. Available from: https://doi.org/10.1097/SLA.0000000000002985

8. Mirili C, Yilmazl A, Demirkan S, Bilicil M, Tekin SB. Clinical significance of prognostic nutritional index (PNI) in malignant melanoma. Int J Clin Oncol. 2019;24:1301-10. Available from: https://doi.org/10.1007/s10147-019-01461-7

9. Geng Y, Qi Q, Sun M, Chen H, Wang P, Chen Z. Prognostic nutritional index predicts survival and correlates with systemic inflammatory response in advanced pancreatic cancer. Eur J Surg Oncol. 2015;41:1508-14. Available from: https://doi.org/10.1016/j.ejso.2015.07.022

10. Zhang L, Ma W, Qiu Z, Kuang T, Wang K, Hu B, et al. Prognostic nutritional index as a prognostic biomarker for gastrointestinal cancer patients treated with immune checkpoint inhibitors. Front Immunol. 2023;14:1219929. Available from: https://doi.org/10.3389/fimmu.2023.1219929

11. Yang H, Liu H, Chen Y, Zhu C, Fang W, Yu Z, et al. Neoadjuvant Chemoradiotherapy Followed by Surgery Versus Surgery Alone for Locally Advanced Squamous Cell Carcinoma of the Esophagus (NEOCRTEC5010): A Phase III Multicenter, Randomized, Open-Label Clinical Trial. J Clin Oncol. 2018;36:2796-803. Available from: https://doi.org/10.1200/jco.2018.79.1483

12. Boggs H, Hanna A, Horiba N, Burrows W, Suntharalingam M. Primary Gross Tumor Volume Is an Important Prognostic Factor in Locally Advanced Esophageal Cancer Patients Treated With Trimodality Therapy. Int J Radiat Oncol Biol Phys. 2014;90:S334-S335. Available from: https://www.redjournal.org/article/S0360-3016(14)01750-7/fulltext

Citation: Zhou X, Wu X, Liu T, Lin S, Luo Z, Wu J, et al. Post-radiation Prognostic Nutritional Index Predicts Survival and Guides Consolidation Chemotherapy in Esophageal Cancer Patients. Int J Radiol Radiat Oncol. 2025;11(1): 001-008. DOI: https://dx.doi.org/10.17352/ijrro.000054

13. Wang ZY, Jiang YZ, Xiao W, Xue XB, Zhang XW, Zhang L. Prognostic impact of tumor length in esophageal cancer: a systematic review and meta-analysis. BMC Cancer. 2021;21:988. Available from: https://doi.org/10.1186/s12885-021-08728-1

14. Zhang HD, Shang XB, Ren P, Gong L, Ahmed A, Ma Z, et al. The predictive value of a preoperative systemic immune-inflammation index and prognostic nutritional index in patients with esophageal squamous cell carcinoma. J Cell Physiol. 2019;234:1794-802. Available from: https://doi.org/10.1002/jcp.27052

15. Song C, Cao J, Zhang F, Wang C, Guo Z, Lin Y, et al. Nutritional risk assessment by scored patient-generated subjective global assessment associated with demographic characteristics in 23,904 common malignant tumors patients. Nutr Cancer. 2019;71:50-60. Available from: https://doi.org/10.1080/01635581.2019.1566478

16. Bozzetti F, Mariani L, Lo Vullo S; SCRINIO Working Group; Amerio ML, Biffi R, et al. The nutritional risk in oncology: a study of 1,453 cancer outpatients. Support Care Cancer. 2012 Aug;20(8):1919-28. Available from: https://doi.org/10.1007/s00520-012-1387-x

17. Bozzetti F, Group SW. Screening the nutritional status in oncology: a preliminary report on 1,000 outpatients. Support Care Cancer. 2009;17:279-84. Available from: https://doi.org/10.1007/s00520-008-0476-3

18. Heneghan HM, Zaborowski A, Fanning M, McHugh A, Doyle S, Moore J, et al. Prospective Study of Malabsorption and Malnutrition After Esophageal and Gastric Cancer Surgery. Ann Surg. 2015;262:803-8. Available from: https://doi.org/10.1097/Sla.0000000000001445

19. Arends J, Bachmann P, Baracos V, Barthelemy N, Bertz H, Bozzetti F, et al. ESPEN guidelines on nutrition in cancer patients. Clin Nutr. 2017;36:11-48. Available from: https://doi.org/10.1016/j.clnu.2016.07.015

20. Guo XW, Liu YC, Gao F, Ji SJ, Zhou JY, Ji L, et al. Pretreatment NRS-2002 scores combined with hematologic inflammation markers are independent prognostic factors in patients with resectable thoracic esophageal squamous cell carcinoma. Cancer Manag Res. 2018;10:2409-18. Available from: https://doi.org/10.2147/CMAR.S167179

21. Wang J, Yu B, Ye Y, Shen J, Ding N, Tang H, et al. Predictive Value of Nutritional Risk Screening 2002 and Prognostic Nutritional Index for Esophageal Cancer Patients Undergoing Definitive Radiochemotherapy. Nutr Cancer. 2018;70:879-85. Available from: https://doi.org/10.1080/01635581.2018.1470656

22. Persson C, Sjoden PO, Glimelius B. The Swedish version of the patient-generated subjective global assessment of nutritional status: gastrointestinal vs urological cancers. Clin Nutr. 1999;18:71-7. Available from: https://doi.org/10.1016/S0261-5614(99)80054-5

23. Quyen TC, Angkatavanich J, Thuan TV, Xuan VV, Tuyen LD, Tu DA. Nutrition assessment and its relationship with performance and Glasgow prognostic scores in Vietnamese patients with esophageal cancer. Asia Pac J Clin Nutr. 2017;26:49-58. Available from: https://doi.org/10.6133/apjcn.122015.02

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;30:1-7. Available from: https://doi.org/10.1093/dote/dox020

25. Conroy T, Galais M-P, Raoul J-L, Bouché O, Gourgou-Bourgade S, Douillard J-Y, et al. Definitive chemoradiotherapy with FOLFOX versus fluorouracil and cisplatin in patients with oesophageal cancer (PRODIGE5/ACCORD17): final results of a randomized, phase 2/3 trial. Lancet Oncol. 2014;15:305-14. Available from: https://doi.org/10.1016/s1470-2045(14)70028-2

26. Chen Y, Guo L, Cheng X, Wang J, Zhang Y, Wang Y, et al. With or without consolidation chemotherapy using cisplatin/5-FU after concurrent chemoradiotherapy in stage II-III squamous cell carcinoma of the esophagus: A propensity score-matched analysis. Radiother Oncol. 2018 Oct;129(1):154-160. Available from: https://doi.org/10.1016/j.radonc.2017.10.031

27. Xia X, Liu Z, Qin Q, Di X, Zhang Z, Sun X, et al. Long-Term Survival in Nonsurgical Esophageal Cancer Patients Who Received Consolidation Chemotherapy Compared With Patients Who Received Concurrent Chemoradiotherapy Alone: A Systematic Review and Meta-Analysis. Front Oncol. 2020;10:604657. Available from: https://doi.org/10.3389/fonc.2020.604657

28. Cox S, Powell C, Carter B, Hurt C, Mukherjee S, Crosby TDL. Role of nutritional status and intervention in oesophageal cancer treated with definitive chemoradiotherapy: outcomes from SCOPE1. Br J Cancer. 2016;115:172-7. Available from: https://doi.org/10.1038/bjc.2016.129

29. Van Cutsem E, Arends J. The causes and consequences of cancer-associated malnutrition. Eur J Oncol Nurs. 2005;9 Suppl 2:S51-63. Available from: https://doi.org/10.1016/j.ejon.2005.09.007

30. Huang YY, Liang SH, Hu Y, Liu X, Ma GW. Prognostic Value of Preoperative Nutritional Assessment and Neutrophil-to-Lymphocyte Ratio in Patients With Thymic Epithelial Tumors. Front Nutr. 2022;9:868336. Available from: https://doi.org/10.3389/fnut.2022.868336

31. Mao YS, Hao SJ, Zou CF, Xie ZB, Fu DL. Controlling Nutritional Status score is superior to Prognostic Nutritional Index score in predicting survival and complications in pancreatic ductal adenocarcinoma: a Chinese propensity score matching study. Br J Nutr. 2020;124:1190-7. Available from: https://doi.org/10.1017/S0007114520002299

32. Shi J, Liu T, Ge Y, Liu C, Zhang Q, Xie H, et al. Cholesterol-modified prognostic nutritional index (CPNI) as an effective tool for assessing the nutrition status and predicting survival in patients with breast cancer. BMC Med. 2023 Dec 21;21(1):512. Available from: https://doi.org/10.1186/s12916-023-03225-7

Citation: Zhou X, Wu X, Liu T, Lin S, Luo Z, Wu J, et al. Post-radiation Prognostic Nutritional Index Predicts Survival and Guides Consolidation Chemotherapy in Esophageal Cancer Patients. Int J Radiol Radiat Oncol. 2025;11(1): 001-008. DOI: https://dx.doi.org/10.17352/ijrro.000054