

Pretreatment prognostic nutritional index is a significant predictor of prognosis in patients with cervical cancer treated with concurrent chemoradiotherapy

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Abstract. This study investigated whether pretreatment neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR) and prognostic nutritional index (PNI) are prognostic factors in patients with cervical cancer who undergo concurrent chemoradiotherapy (CCRT) and radiotherapy (RT). A total of 131 patients who underwent CCRT and RT for cervical cancer were retrospectively investigated and the correlations of NLR, PLR and PNI with clinical parameters and prognosis were assessed in CCRT and RT. The CCRT and RT groups had a median progression-free survival (PFS) of 41.82 and 24.72 months, respectively, and an overall survival of 49.70 and 29.56 months, respectively. At a cut-off value of $NLR \geq 2.85$, the PFS and OS in patients with higher NLR undergoing RT were significantly shorter compared with those in patients with lower NLR ($P=0.029$ and $P=0.017$, respectively). At a cut-off value for PNI of ≤ 48.55 in patients undergoing CCRT and ≤ 45.80 in patients undergoing RT, the PFS and OS in patients with lower PNI were significantly shorter compared with those in patients with higher PNI (PFS and OS with CCRT, $P<0.001$ and $P<0.001$, respectively; PFS and OS with RT, $P=0.002$ and $P=0.008$, respectively). Multivariate analyses also identified low PNI as an independent prognostic factor for PFS and OS in patients receiving CCRT. Therefore, low PNI was shown to predict poor prognosis in patients with cervical cancer.

Introduction

Cervical cancer is the fourth most common malignancy among women worldwide (1), with a 5-year recurrence rate of 28% according to the International Federation of Gynecology and Obstetrics (FIGO) (2). Poor prognostic factors for cervical cancer include stage, tumor size, histology and lymph node (LN) metastasis (3,4). However, these parameters are not sufficient to accurately predict prognosis.

Systemic inflammatory response (SIR) is an important prognostic factor for survival in various types of cancer (5,6). Neutrophils, platelets, lymphocytes and albumin play a prominent role in cancer-related inflammation. Recent evidence has indicated that relative differences in neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR) and prognostic nutritional index (PNI) ($PNI=10 \times$ albumin concentration $+0.005 \times$ total lymphocyte count) affect SIR and, consequently, cancer survival (7-10). Hypoalbuminemia is often observed in patients with advanced cancer and is usually considered to be a marker of malnutrition and cachexia. It has also been reported that albumin is involved in SIR and survival in various types of cancer (11,12). Although pretreatment NLR and PLR have been shown to predict outcome in gynecological cancers, such as endometrial (13,14), cervical (15,16) and ovarian cancer (17,18), PNI has not been shown to be a predictive factor in patients with cervical cancer. The aim of this study was to investigate the correlation between pretreatment NLR, PLR, PNI and prognosis in patients who had been treated with concurrent chemoradiotherapy (CCRT) or radiotherapy (RT) for cervical cancer.

Patients and methods

Patients. The study population consisted of 131 patients with primary cervical cancer who underwent CCRT or RT at the Department of Obstetrics and Gynecology of Okayama University Hospital (Okayama, Japan) between April, 2007 and March, 2013. The study protocol was approved by the Institutional Review Board of Okayama University Hospital. The patients' clinical data, including medical history, physical

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examination and clinical staging, were reviewed. Computed tomography (CT) and positron emission tomography-CT are widely accepted modalities for assessing the extent of LN metastasis; according to traditional criteria, LNs with short-axis length of >10.0 mm are defined as metastatic (19). The baseline pretreatment characteristics (stage, histology, LN metastasis, parametrial involvement, vaginal invasion and maximum tumor size) of the patients are listed in Table I.

Laboratory analysis. All the patients had their white blood cell (WBC) count and albumin levels recorded within 1 week prior to treatment. Differential WBC counts and albumin levels were measured prior to treatment with RT or CCRT; WBC, neutrophil, lymphocyte and platelet counts were measured using automated blood cell counters (Bayer HealthCare, Diagnostics Division, Tarrytown, NY, USA). The levels of serum albumin were measured by latex nephelometry (LT Auto Wako, Osaka, Japan). NLR was defined as the absolute neutrophil count (μl) divided by the absolute lymphocyte count (μl), and PLR was defined as the absolute platelet count (μl) divided by the lymphocyte count (μl). The PNI was calculated as previously described (20). Briefly, PNI was defined as $10 \times$ albumin concentration (g/dl) + 0.005 \times total lymphocyte count (μl). During RT or CCRT, the WBC, neutrophil, lymphocyte and platelet counts, albumin levels and weight were measured weekly. Acute toxicities were evaluated and graded using the Common Terminology Criteria for Adverse Events (CTCAE) version 4.0 (21). Seven toxicities, including leukopenia, neutropenia, lymphocytopenia, thrombocytopenia, weight loss, diarrhea and hyponatremia, were recorded based on CTCAE v.4.0.

Treatment. The patients were treated with a combination of external irradiation and intracavitary brachytherapy (ICBT) with curative intent. RT was delivered at 2.0 Gy per fraction once daily, 5 days per week, over 5 weeks. The median dose to the whole pelvis was 50.0 Gy and ICBT as the high dose rate was 24 Gy/4 times. For CCRT, the patients were treated with either cisplatin (CDDP; 40 mg/m² infusion weekly for six cycles), nedaplatin (NED; 30 mg/m² infusion weekly for eight cycles), or ifosfamide plus NED (IN) [ifosfamide (1 g/m²) infusion on days 1-5 and NED (80 mg/m²) infusion on day 1 of a 3-week cycle, for three cycles], as previously described (22,23). A total of 52 patients treated with CDDP, 28 treated with NED and 15 treated with IN chemotherapy were evaluated. The remaining 36 patients did not receive concurrent chemotherapy due to the presence of comorbidities or advanced age (≥ 75 years). CCRT was interrupted for up to 1 week in patients with WBC counts <2,000/ μl , neutrophil counts <1,000/ μl , or platelet counts <75,000/ μl . If these side effects persisted for >1 week, no additional chemotherapy was administered. RT was suspended indefinitely in patients who exhibited a WBC count <1,000/ μl , neutrophil count <500/ μl , or platelet count <25,000/ μl . Since the prognosis of patients with cervical cancer is associated with their hemoglobin (Hb) level during RT or CCRT (24), our treatment policy is to administer red blood cell transfusions prior to and during CCRT if the Hb level is <10.0 g/dl, until it exceeds 10 g/dl. Patients underwent follow-up examinations approximately every 1-2 months for the first 6 months, every 3 months for the next 2 years, and every 6 months thereafter.

Statistical analysis. Statistical analyses were performed using the χ^2 test and the Mann-Whitney U test for comparisons with the controls and the one-factor analysis of variance, followed by Fisher's protected least-significant difference test for all pairwise comparisons. The survival curves were calculated by the Kaplan-Meier method; differences in the recurrence or survival curves were examined using the log-rank test. The analyses were performed using the SPSS software, version 20.0 (IBM SPSS, Armonk, NY, USA). $P < 0.05$ was considered to indicate statistically significant differences.

Results

Patient characteristics. The clinicopathological characteristics, including patient age, tumor stage, histology, LN metastasis, parametrial involvement, vaginal invasion, maximum tumor size and therapy, are listed in Table I. The mean values in the CCRT group (n=95) were as follows: NLR=3.17 (range, 0.89-9.52); PLR=188.29 (range, 40.61-466.49); and PNI=49.83 (range, 39.15-62.80). The mean values in the RT group (n=36) were as follows: NLR=3.05 (range, 1.15-8.05); PLR=183.40 (range, 74.88-533.22); and PNI=47.41 (range, 30.34-56.10).

The distribution of these three values according to the patients' clinical characteristics is shown in Table II. In the CCRT group, PLR was found to be significantly associated with LN metastasis ($P < 0.001$) and vaginal invasion ($P = 0.005$), whereas PNI was significantly associated with stage ($P = 0.004$), LN metastasis ($P = 0.031$), parametrial involvement ($P = 0.011$) and vaginal invasion ($P = 0.027$). In the RT group, NLR was significantly associated with stage ($P = 0.041$), histology ($P = 0.012$), maximum tumor size ($P = 0.013$), parametrial involvement ($P < 0.001$) and vaginal invasion ($P = 0.044$); PLR was associated with FIGO stage ($P = 0.030$), histology ($P = 0.008$), maximum tumor size ($P = 0.005$) and parametrial involvement ($P = 0.016$); and PNI was associated with histology ($P = 0.018$), LN metastasis ($P = 0.010$), maximum tumor size ($P = 0.001$) and parametrial involvement ($P < 0.001$; Mann-Whitney U test, $P < 0.05$).

Overall, the CCRT group had a median progression-free survival (PFS) of 41.82 months and an overall survival (OS) of 49.70 months; at the last follow-up, 59 patients in the CCRT group remained alive with no evidence of disease, 28 had succumbed to the disease and 8 were alive with disease. In the RT group, the median PFS was 24.72 months and the OS was 29.56 months; at the last follow-up, 22 patients remained alive with no evidence of disease, 13 had succumbed to the disease and 1 was alive with disease.

Receiver operating characteristic curve analyses were used to determine the optimal cut-off values of NLR, PLR and PNI to predict recurrence (PFS) and survival (OS). The analyses identified $\text{NLR} \geq 2.78$ [area under the curve (AUC)=0.635, sensitivity: 63.9%, specificity: 49.2%], $\text{PLR} \geq 172.50$ (AUC=0.597, sensitivity: 58.3%, specificity: 55.9%) and $\text{PNI} \leq 48.55$ (AUC=0.720, sensitivity: 72.9%, specificity: 58.3%) as the most accurate cut-off values for predicting recurrence (PFS) in the CCRT group. The analyses identified $\text{NLR} \geq 2.85$ (AUC=0.679, sensitivity: 66.7%, specificity: 66.7%), $\text{PLR} \geq 128.00$ (AUC=0.829, sensitivity: 80.0%, specificity: 52.4%) and $\text{PNI} \leq 45.80$ (AUC=0.876, sensitivity: 85.7%,

Table I. Patient and tumor characteristics.

Baseline characteristics	All patients, no. (%)	
Age at diagnosis, years [mean (range)]	61.5 (25-88)	
Stage	61.5 (25-88)	
Ib1	7	5.8
Ib2	10	8.3
IIa1	7	5.8
IIa2	4	3.3
IIb	51	42.1
IIIa	3	2.5
IIIb	33	27.3
IVa	6	4.9
Histology		
SCC	104	85.9
AD	14	11.6
ADSQ	3	2.5
Lymph node metastasis		
Negative	83	68.6
Positive	38	31.4
Parametrial invasion		
Negative	30	24.8
Positive	91	75.2
Vaginal invasion		
Negative	63	52.1
Positive	58	47.9
Maximum tumor size, cm		
≤4.0	41	33.9
>4.0	80	66.1
Treatment		
CCRT	95	78.5
RT	36	21.5
Chemotherapy regimen (N=95)		
Weekly CDDP	52	54.7
Weekly NED	28	29.4
Ifosfamide + NED	15	15.9

CDDP, cisplatin; NED, nedaplatin; CCRT, concurrent chemoradiotherapy; RT, radiotherapy; SCC, squamous cell carcinoma; AD, adenocarcinoma; ADSQ, adenosquamous carcinoma.

specificity: 60.0%) as the most accurate cut-off values for predicting recurrence (PFS) in the RT group.

The analyses identified $NLR \geq 2.78$ (AUC=0.616, sensitivity: 60.7%, specificity: 47.8%), $PLR \geq 171.00$ (AUC=0.609, sensitivity: 60.7%, specificity: 50.7%), and $PNI \leq 48.55$ (AUC=0.736, sensitivity: 73.1%, specificity: 64.3%) as the most accurate cut-off values for predicting survival (OS) in the CCRT group. The analyses identified $NLR \geq 2.85$ (AUC=0.724, sensitivity: 71.4%, specificity: 68.2%), $PLR \geq 130.00$ (AUC=0.792, sensitivity: 78.6%, specificity: 50.0%) and $PNI \leq 45.80$

(AUC=0.851, sensitivity: 86.4%, specificity: 57.1%), as the most accurate cut-off values for predicting survival (OS) in the RT group (Fig. 1).

The correlations between clinical factors and recurrence (PFS) or survival (OS) were assessed in univariate and multivariate analyses (Tables III and IV). In the univariate analysis, LN metastasis (P=0.032), histology (P=0.006), maximum tumor size (P=0.013), PNI (P=0.002) and extended radiation duration (>6 weeks; P=0.036) were significantly associated with recurrence (PFS) in the CCRT group. Moreover, histology (P=0.016), maximum tumor size (P=0.045) and PNI (P=0.012) were independent predictors of recurrence (PFS) in the CCRT group on multivariate analysis. Univariate analysis suggested that LN metastasis (P=0.013), histology (P=0.012), PNI (P=0.001) and extended radiation duration (P=0.016) were significantly associated with OS in the CCRT group. Moreover, histology (P=0.010) and PNI (P=0.003) were independent predictors of OS in the CCRT group.

In the RT group, univariate analysis suggested that stage (P=0.014), LN metastasis (P=0.007), maximum tumor size (P=0.005), NLR (P=0.029), PNI (P=0.002) and extended radiation duration (P<0.001) were significantly associated with recurrence (PFS). Moreover, maximum tumor size (P=0.030) and extended radiation duration (P=0.019) were independent predictors of recurrence (PFS) in the RT group. Univariate analysis suggested that stage (P=0.015), LN metastasis (P=0.009), maximum tumor size (P=0.008), NLR (P=0.017), PNI (P=0.008) and extended radiation duration (P<0.001) were significantly associated with OS in the RT group. Moreover, extended radiation duration (P<0.001) were independent predictors of OS in the RT group.

Discussion

In cervical cancer, stage, tumor size, histological type, presence of lymphovascular invasion and metastasis to the regional LNs at the time of diagnosis are significant prognostic factors (3,4). However, the prognostic value of SIR in cervical cancer remains unknown. To the best of our knowledge, this is the first study to evaluate whether NLR, PLR and PNI are predictors of poor prognosis for patients with cervical cancer treated with CCRT or RT.

Neutrophils release inflammatory cytokines, leukocyte chemotactic factors and other phagocytic mediators that may damage cellular DNA, inhibit apoptosis and promote angiogenesis (25-28). Platelets release potent mitogens or adhesive glycoproteins, such as platelet-derived growth factor, transforming growth factor- β and vascular endothelial growth factor (29-31). The albumin levels decrease with increased levels of pro-inflammatory cytokines, such as interleukin (IL)-1, IL-6 and tumor necrosis factor, which modulate albumin production (32). Lymphocytes, such as CD3⁺ T cells and natural killer cells may affect tumor growth and metastasis (33). Recent evidence has shown that relative differences in neutrophil, platelet and lymphocyte counts, albumin levels, NLR, PLR, and PNI, are systemic indicators of prognosis. PNI is based on albumin and absolute lymphocyte count, which are measured routinely in clinical practice, and it is designed to assess nutritional and immunological status, which may predict prognosis (34). Mizunuma *et al* reported that NLR was

Table II. Associations of NLR, PLR and PNI with clinical factors in cervical cancer.

A, CCRT							
Variables	N	NLR	P-value	PLR	P-value	PNI	P-value
Stage			0.216		0.158		0.004 ^a
I-II	67	3.05±1.46		179.29±70.98		50.65±4.50	
III-IV	28	3.49±1.81		209.81±102.60		47.86±3.73	
Histology			0.089		0.208		0.471
SCC	86	3.23±1.63		191.73±83.88		49.67±4.40	
Non-SCC	9	2.67±0.77		155.37±57.34		48.54±5.02	
LNM			0.056		<0.001 ^a		0.031 ^a
Negative	57	2.92±1.43		162.82±62.51		50.63±4.25	
Positive	38	3.55±1.73		226.48±93.58		48.63±4.54	
MTS, cm			0.154		0.233		0.089
≤4.0	24	2.78±1.42		170.95±72.65		51.17±4.48	
>4.0	71	3.31±1.61		194.15±84.86		49.38±4.39	
PI			0.506		0.155		0.011 ^a
Negative	20	3.00±1.19		169.06±60.55		52.04±3.69	
Positive	75	3.22±1.67		193.41±86.69		49.24±4.48	
VI			0.229		0.005 ^a		0.027 ^a
Negative	48	2.98±1.34		165.19±68.46		50.82±4.28	
Positive	47	3.37±1.77		211.88±88.84		48.81±4.44	
B, RT							
Variables	N	NLR	P-value	PLR	P-value	PNI	P-value
Stage			0.041 ^a		0.030 ^a		0.018 ^a
I-II	21	2.58±1.55		151.11±53.27		49.38±5.61	
III-IV	15	3.70±1.59		228.61±119.62		44.65±5.76	
Histology			0.012 ^a		0.008 ^a		0.109
SCC	28	3.31±1.74		198.00±100.48		46.77±6.55	
Non-SCC	8	2.16±0.79		132.29±38.12		49.65±3.42	
LNM			0.114		0.078		0.010 ^a
Negative	26	2.78±1.66		158.49±54.16		48.97±5.36	
Positive	10	3.75±1.46		248.16±140.72		43.37±6.20	
MTS, cm			0.013 ^a		0.005 ^a		0.001 ^a
≤4.0	17	2.35±0.84		139.37±36.57		50.62±4.67	
>4.0	19	3.68±1.94		222.79±112.00		44.54±5.81	
PI			<0.001 ^a		0.016 ^a		<0.001 ^a
Negative	10	1.96±0.72		140.77±36.30		51.83±3.26	
Positive	26	3.47±1.71		199.79±104.42		45.71±6.08	
VI			0.044 ^a		0.076		0.249
Negative	15	2.40±1.70		153.01±62.18		48.81±6.18	
Positive	21	3.51±1.48		205.11±107.64		46.42±5.94	

^aP<0.0. CCRT, concurrent chemoradiotherapy; RT, radiotherapy; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; PNI, prognostic nutritional index; LNM, lymph node metastasis; MTS, maximum tumor size; PI, parametrial involvement; VI, vaginal invasion; SCC, squamous cell carcinoma.

a significant prognostic factor for PFS and OS in patients with cervical cancer treated with CCRT or RT (15).

We investigated whether pretreatment clinicopathological parameters were correlated with NLR, PLR and PNI, which

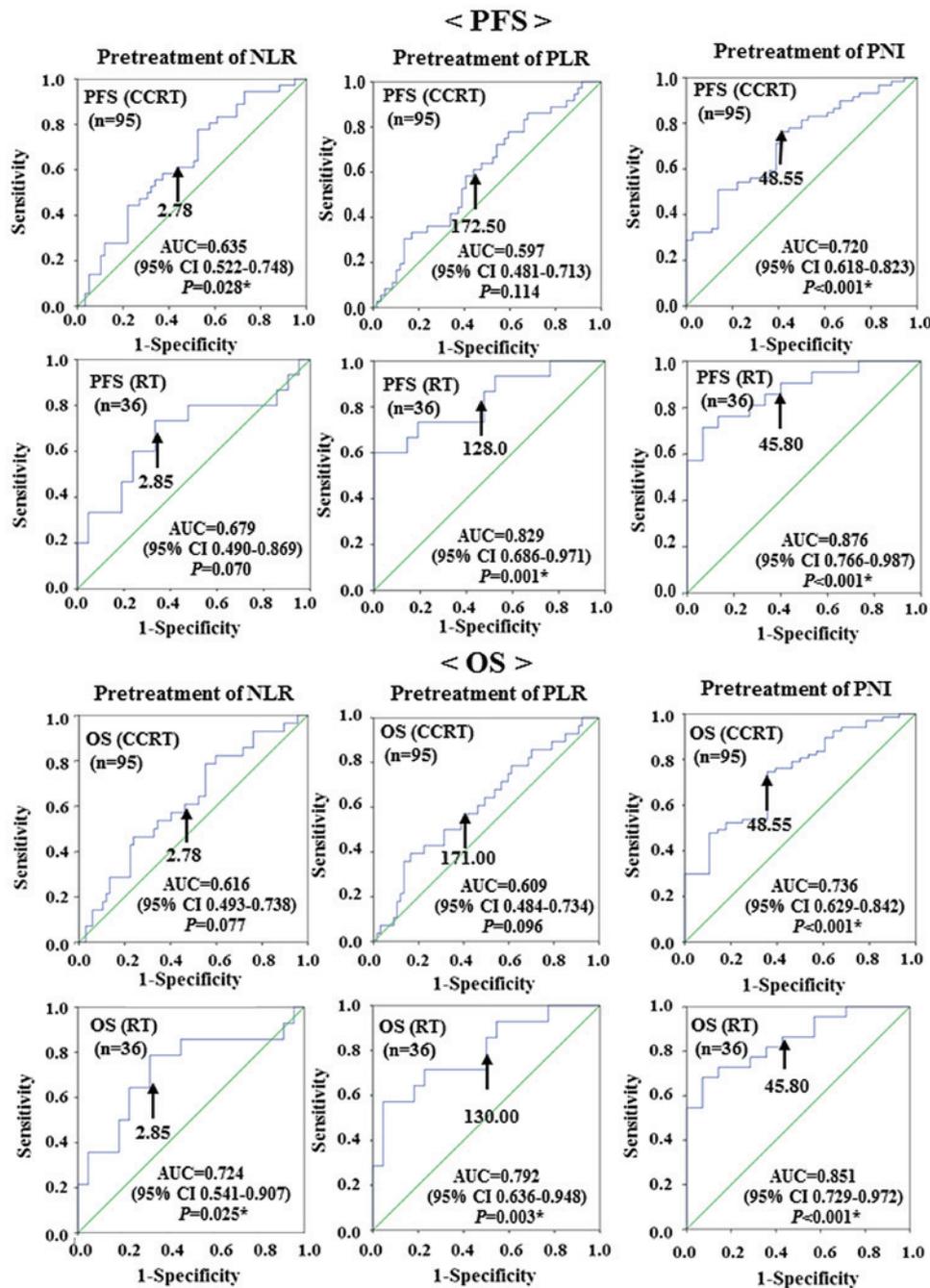


Figure 1. Receiver operating characteristic curve analysis determining the optimal cut-off values for NLR, PLR and PNI to predict recurrence (PFS) and survival (OS) in patients with cervical cancer treated with CCRT (n=95) or with RT (n=36). The optimal cut-off values for predicting recurrence (PFS) in the CCRT group were as follows: NLR=2.78 (AUC=0.635; 95% CI: 0.522-0.748; P=0.028); PLR=172.50 (AUC=0.597; 95% CI: 0.481-0.713; P=0.114); and PNI=48.55 (AUC=0.720; 95% CI: 0.618-0.823; P<0.001). The optimal cut-off values for predicting recurrence (PFS) in the RT group were as follows: NLR=2.85 (AUC=0.679; 95% CI: 0.490-0.869; P=0.070); PLR=128.00 (AUC=0.829; 95% CI: 0.686-0.971; P=0.001); and PNI=45.80 (AUC=0.876; 95% CI: 0.766-0.987; P<0.001). The optimal cut-off values for predicting survival (OS) in the CCRT group were as follows: NLR=2.78 (AUC=0.616; 95% CI: 0.493-0.738; P=0.077); PLR=171.00 (AUC=0.609; 95% CI: 0.484-0.734; P=0.096); and PNI=48.55 (AUC=0.736; 95% CI: 0.629-0.842; P<0.001). The optimal cut-off values for predicting survival (OS) in the RT group were as follows: NLR=2.85 (AUC=0.724; 95% CI: 0.541-0.907; P=0.025); PLR=130.00 (AUC=0.792; 95% CI: 0.636-0.948; P=0.003); and PNI=45.80 (AUC=0.851; 95% CI: 0.729-0.972; P<0.001). PFS, progression-free survival; OS, overall survival; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; PNI, prognostic nutritional index; CCRT, concurrent chemoradiotherapy; RT, radiotherapy; AUC, area under the curve; CI, confidence interval.

reflect SIR. In the CCRT group, PLR was significantly associated with LN metastasis and vaginal invasion; and PNI was significantly associated with stage, LN metastasis, parametrial involvement and vaginal invasion. In the RT group, NLR was significantly associated with stage, histology, maximum tumor size, parametrial involvement and vaginal invasion; PLR

was associated with stage, histology, maximum tumor size and parametrial involvement; and PNI was associated with stage, LN metastasis, maximum tumor size and parametrial involvement.

The present study mainly aimed to evaluate the correlation of certain parameters, such as NLR, PLR and PNI,

Table III. Prognostic factors for progression-free survival and overall survival in cervical cancer patients who underwent CCRT (n=95) by Cox's multivariate analysis.

Factors	Progression-free survival						Overall survival					
	Univariate analysis			Multivariate analysis			Univariate analysis			Multivariate analysis		
	HR	(95% CI)	P-value	HR	(95% CI)	P-value	HR	(95% CI)	P-value	HR	(95% CI)	P-value
Stage	1.397	(0.707-2.758)	0.336				1.335	(0.616-2.895)	0.464			
Lymph node metastasis	2.049	(1.064-3.947)	0.032 ^a	1.485	(0.764-2.888)	0.244	2.612	(1.222-5.585)	0.013 ^a	2.019	(0.936-4.354)	0.073
Histology	0.313	(0.137-0.717)	0.006 ^a	0.356	(0.153-0.824)	0.016 ^a	0.315	(0.127-0.779)	0.012 ^a	0.300	(0.120-0.751)	0.010 ^a
Maximum tumor size	4.510	(1.382-14.715)	0.013 ^a	3.401	(1.027-11.267)	0.045 ^a	3.270	(0.987-10.835)	0.053			
Parametrial involvement	1.803	(0.701-4.638)	0.221				1.757	(0.609-5.065)	0.297			
Vaginal invasion	0.803	(0.416-1.550)	0.513				1.275	(0.606-2.680)	0.522			
NLR	1.423	(0.728-2.783)	0.303				1.536	(0.717-3.289)	0.269			
PLR	1.522	(0.784-2.954)	0.215				1.634	(0.753-3.543)	0.214			
PNI	2.796	(1.438-5.437)	0.002 ^a	2.380	(1.212-4.676)	0.012 ^a	3.754	(1.726-8.161)	0.001 ^a	3.273	(1.481-7.237)	0.003 ^a
Leukopenia (grade 4)	0.858	(0.303-2.427)	0.772				1.126	(0.390-3.248)	0.827			
Neutropenia (grade 4)	0.047	(0.000-78.691)	0.419				0.047	(0.000-219.951)	0.478			
Lymphocytopenia (grade 4)	0.874	(0.430-1.776)	0.709				1.022	(0.462-2.258)	0.958			
Thrombocytopenia (grade 4)	1.853	(0.445-7.720)	0.397				2.102	(0.498-8.861)	0.312			
Weight loss (grade ≥2)	1.072	(0.446-2.577)	0.876				1.211	(0.460-3.187)	0.699			
Diarrhea (grade ≥3)	0.742	(0.288-1.909)	0.535				0.940	(0.356-2.485)	0.901			
Hyponatremia(grade ≥3)	1.090	(0.545-2.179)	0.808				1.621	(0.757-3.470)	0.214			
ERD (>6 weeks)	2.322	(1.056-5.105)	0.036 ^a	1.799	(0.814-3.976)	0.147	2.893	(1.221-6.852)	0.016 ^a	2.096	(0.887-4.952)	0.092

^aP<0.05. CCRT, concurrent chemoradiotherapy; NLR, neutrophil/lymphocyte ratio; PLR, platelet/lymphocyte ratio; PNI, prognostic nutritional index; ERD, extension of radiation duration; HR, hazard ratio; CI, confidence interval.

Table IV. Clinical factors affecting progression-free and overall survival in cervical cancer patients who underwent RT (n=36) by Cox's multivariate analysis.

Factors	Progression-free survival						Overall survival					
	Univariate analysis			Multivariate analysis			Univariate analysis			Multivariate analysis		
	HR	(95% CI)	P-value	HR	(95% CI)	P-value	HR	(95% CI)	P-value	HR	(95% CI)	P-value
Stage	3.846	(1.308-11.310)	0.014 ^a	0.603	(0.114-3.197)	0.552	4.263	(1.331-13.652)	0.015 ^a	0.757	(0.129-4.444)	0.758
Lymph node metastasis	4.091	(1.472-11.370)	0.007 ^a	1.919	(0.383-9.610)	0.428	4.101	(1.413-11.904)	0.009 ^a	1.459	(0.270-7.885)	0.661
Histology	1.134	(0.320-4.021)	0.846				1.040	(0.289-3.742)	0.952			
Maximum tumor size (>4.0 cm)	18.773	(2.457-143.465)	0.005 ^a	11.976	(1.263-1,013.546)	0.030 ^a	15.656	(2.044-119.908)	0.008 ^a	8.072	(0.873-74.642)	0.066
Parametrial involvement	3.075	(0.691-13.674)	0.140				2.850	(0.635-12.788)	0.172			
Vaginal invasion	1.639	(0.559-4.803)	0.368				1.922	(0.601-6.140)	0.271			
NLR	3.587	(1.139-11.292)	0.029 ^a	0.724	(0.158-3.321)	0.678	4.766	(1.324-17.154)	0.017 ^a	1.682	(0.342-8.261)	0.522
PLR	3.059	(0.862-10.858)	0.084				2.660	(0.741-9.547)	0.133			
PNI	5.315	(1.8741-5.074)	0.002 ^a	3.127	(0.944-10.356)	0.062	4.219	(1.456-12.228)	0.008 ^a	1.783	(0.551-5.764)	0.334
Lymphocytopenia (grade 4)	0.047	(0.000-16,748.526)	0.639				0.047	(0.000-25,878.809)	0.651			
Weight loss (grade ≥2)	2.770	(0.770-9.965)	0.119				2.775	(0.762-10.106)	0.122			
Diarrhea (grade ≥3)	1.828	(0.238-14.027)	0.562				1.940	(0.251-14.981)	0.525			
Hyponatremia (grade ≥3)	2.467	(0.875-6.959)	0.088				2.635	(0.913-7.605)	0.073			
ERD (>6 weeks)	10.637	(3.071-36.843)	<0.001 ^a	5.888	(1.332-26.026)	0.019 ^a	13.439	(3.515-51.378)	<0.001 ^a	4.853	(1.044-22.558)	0.044 ^a

^aP<0.05. RT, radiotherapy; NLR, neutrophil/lymphocyte ratio; PLR, platelet/lymphocyte ratio; PNI, prognostic nutritional index; ERD, extension of radiation duration; HR, hazard ratio; CI, confidence interval.

with recurrence and survival in cervical cancer patients who underwent CCRT or RT. In the CCRT group, the PFS and OS of patients with lower PNI were significantly worse compared with those of patients with higher PNI. Multivariate analysis identified PNI as an independent prognostic factor for both PFS and OS. In the RT group, the PFS and OS of patients with higher NLR were significantly shorter compared with those of patients with lower NLR; and the PFS and OS of patients with lower PNI were significantly shorter compared with those of patients with higher PNI. Furthermore, PNI was found to be superior to NLR and PLR as a predictor of survival in the CCRT group.

There were certain limitations to our study, including the limited number of patients and the relatively short duration of follow-up. Further prospective studies with more patients and longer follow-up periods would provide more definitive data to elucidate the significance of our findings.

In conclusion, our results demonstrated that the determination of PNI may serve as a useful indicator of prognosis in cervical cancer patients who undergo CCRT.

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